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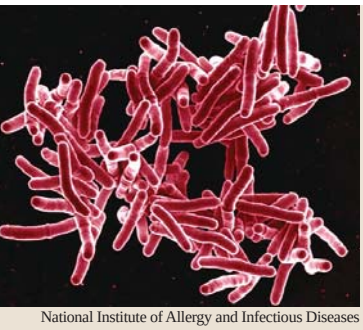

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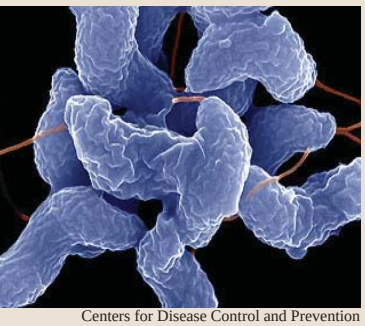

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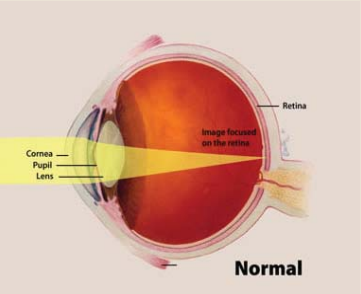

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Development and Implementation of a Cohort Review for Latent Tuberculosis Infection

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The Centers for Disease Control and Prevention (CDC) recommends that, in low-incidence settings for tuberculosis (TB), health departments periodically review their cases of latent TB infection (LTBI). The objective of this study was to evaluate the design and implementation of an LTBI cohort review that can be used to assess program performance. The methods used for the LTBI cohort review were developed and modified from those described previously by the CDC for TB disease. A stratified random sample of LTBI cases was selected from three U.S. Army installations to compare program outcomes. A total of 295 TB tests were performed on 215 patients. Sixty-one (76%) of the 80 repeat tests performed were positive. Of the 194 patients who were recommended therapy, 146 (75%) initiated therapy and 114 (59%) completed therapy. The U.S. Army's TB control program can be improved by reducing unnecessary testing of low-risk groups, increasing completion of LTBI treatment, reducing treatment delays, and ensuring data accuracy. The LTBI cohort review should be performed at least annually at the installation level to improve the quality of TB control programs.

The tuberculosis (TB) cohort review is a systematic review of the management of patients with TB disease. It is an essential component of the TB control program promulgated by the Centers for Disease Control and Prevention (CDC). The goal of the TB cohort review is to contribute toward the elimination of TB by ensuring accountability of program outcomes.[1,2]

Settings with low TB incidence, defined as a rate ≤3.5 cases per 100,000 population,[3] have unique challenges for TB control compared to areas with higher incidence. These challenges include loss of case management expertise, loss of funding and personnel, long distances separating patients from TB care providers, and possible elimination of the TB control program altogether. The U.S. Army reported only two incident cases of TB disease among active component service members in 2011, a rate of 0.4 per 100,000 population.[4,5] The U.S. military has serious challenges to TB control similar to other low-incidence populations, as well as the additional challenges of worldwide geographic dispersion of military installations, frequent turnover of medical staff, service member deployments to TB-endemic areas, and service member residence in congregate settings. Despite these challenges, a 2011 cohort review of the cases in the U.S. Army suggested that performance indicators for the management of TB disease exceeded national averages and CDC benchmarks in most areas.[5] However, there were also areas that did not meet performance targets, including time to diagnosis, implementation of targeted testing, and use of genotyping and other modern TB surveillance tools.

A critical element of TB control and prevention in low-incidence settings is finding and managing cases of latent TB infection (LTBI).[3] To evaluate the effectiveness of LTBI management, CDC recommends that, in settings where there are 15 or fewer cases of TB disease annually, control programs focus additional cohort review efforts on patients with LTBI.[6] However, even in low-incidence settings, LTBI cohort reviews have not been widely used. Furthermore, although the methods of cohort review for TB disease are well established,[1] methods for conducting LTBI cohort reviews have not yet been established or reported in the literature. The objective of this study was to evaluate the design and implementation of an LTBI cohort review that can be used to assess program performance.

METHODS

LTBI cases among active component soldiers occurring at three U.S. Army installations were chosen for the analysis: Fort Drum, NY; Fort Benning, GA; and Tripler Army Medical Center (TAMC), Honolulu, HI. The three sites were chosen for their heterogeneous settings. Fort Drum had large numbers of troops returning from military service in Iraq and Afghanistan. Fort Benning has a large population of recruits entering military service for basic military training. TAMC is a large military hospital caring for service members and other military beneficiaries from Hawaii and throughout the Pacific region. During the time period covered in this review, TAMC was also known to be the only U.S. Army installation using an interferon-gamma release assay (IGRA), specifically QuantiFERON® Gold-in-Tube, for routine testing for LTBI. The other installations routinely used the tuberculin skin test (TST).

Records for all LTBI cases identified during 1 January 2011 through 30 April 2012 were obtained for all patients known to each installation's preventive medicine service who had a positive TST or IGRA

at that installation, a referral for a positive test performed at another installation, or a referral for completion of a previously initiated course of treatment. Cases were included if they had a positive test at any time during military service but had no history of previously completed treatment. A stratified random sample of the cases from each installation was then taken to obtain equal numbers of participants at each location by using a random number generator and then stratifying by installation. Patients with a positive test who did not return for provider evaluation were excluded from analysis. Service members who were not in the active component of the U.S. military were excluded because their complete healthcare data were unavailable. Case records were then reviewed in detail using the military's electronic medical record, the Armed Forces Health Longitudinal Technology Application (AHLTA); and the U.S. Army electronic TB test registry, the Medical Protection System (MEDPROS). The tests performed at time of the evaluation by the installation's preventive medicine service were used to determine eligibility for this analysis. If no test was performed at that installation, then the test performed at the previous installation was used.

The data collection instrument used for this LTBI cohort review was developed and modified from those described previously by CDC for TB disease.[1] It included demographics; clinical, radiographic, and laboratory case characteristics; deployment and travel history; and treatment adherence and other outcomes. Diagnostic criteria recommended by CDC were used to interpret the tuberculin skin test (TST) and IGRA results.[7,8] LTBI performance targets were modeled after those from national performance targets established for TB disease by the CDC.[9,10] These performance targets included an assessment of whether testing was indicated, the results of repeat testing (usually performed to "confirm" the diagnosis of LTBI), the proportion of cases who initiated and completed treatment, the time to diagnosis and treatment, and an evaluation of data completeness and accuracy.

STATA 11.1 (StataCorp, College Station, TX) was used for all analyses. Risk ratios, chi-square, and Fisher's exact tests were used to assess heterogeneity of categorical outcomes. T-tests or analysis of variance tests were used to assess differences for continuous outcomes. Kaplan-Meier analysis and log-rank tests were used to compare time to treatment between groups. Institutional Review Board approval was received from the Walter Reed Army Institute of Research.

RESULTS

More than 63,000 TB tests for LTBI were performed at the three installations during the 16-month study period. The overall prevalence and incidence of LTBI could not be calculated because the available data did not specify whether the tests were initial or subsequent tests. Among those tested, more than 1,000 tests were positive. A stratified sample of 215 positive service members was selected for analysis from the three sites. Characteristics of the study patients are displayed in **Table 1.** These characteristics were reflective of the heterogeneity between the populations and missions of the installations. For example, individuals from TAMC were more likely to be female, officers, and healthcare workers. In contrast, service members from Fort Benning, a basic training installation, were less likely to have been deployed and more likely to have been TST positive identified at entry into service. All but two (1%) of those with positive tests for LTBI had a chest X-ray performed, and, although 4% had abnormal chest x-rays, none were found to have TB disease.

Altogether, 295 TB tests were performed on the 215 service members during their evaluation by the three installation preventive medicine services. Many patients had one or more tests performed at previous installations, but those test results were not included in this analysis. **Table 2** shows that the top three reasons for testing were deployment (38%), accession (24%), and confirmation of a previous positive test (22%). **Table 2** also shows an assessment of whether testing was indicated according to either U.S. Army policy[11,12] or CDC guidelines for targeted testing.[13,14] A little more than half (54%) of the tests were indicated according to U.S. Army policy at the time, but only 7% according to CDC guidelines.

TABLE 1. Characteristics of the study population

Category	Fort Drum N=74		Fort Benning N=70		TAMC N=71		p-value	N=215	
Mean age (SD)	28.7	6.4	30	8.3	30.4	7.4	0.32	29.7	7.4
Male	70	95%	66	94%	58	82%	0.01	194	90%
Enlisted	70	95%	63	90%	54	76%	0.004	187	87%
Occupation									
Health care	3	4%	8	11%	14	20%	0.007	25	12%
Military police	1	1%	0	0	1	1%	1	2	1%
Combat arms	21	28%	31	44%	13	19%	0.003	65	30%
Foreign born	25	34%	39	56%	30	42%	0.03	94	44%
History of deployment	66	89%	30	43%	60	85%	<0.0001	156	73%
History of BCG vaccine	21	28%	19	27%	15	21%	0.57	55	26%
First positive TB test									
Entry into service	17	23%	39	56%	15	21%	<0.0001	71	33%
During service	57	77%	31	44%	56	79%	–	144	67%

BCG=Bacille Calmette-Guérin vaccine, SD=standard deviation, TAMC=Tripler Army Medical Center, TB=tuberculosis

TABLE 2. Documented indication for testing for latent tuberculosis infection

	Army policy		CDC guidelines		Total no. tested
Entry into service[a]	70	100%	7	10%[b]	70
Deployment testing	73	66%	0	0	111
Contact investigation	2	100%	2	100%	2
Administrative[c]	0	0	0	0	44
Occupational	4	100%	4	100%	4
Confirmatory testing[d]	9	14%	9	14%	64
Total	158	54%	22	7%	295

CDC=Centers for Disease Control and Prevention
[a]Army policy at the time of the study was tuberculin skin test in all new recruits.[11] It has since been changed to targeted testing.[15]
[b]Estimated based on Ref. 21.
[c]Documented as "routine," "required for physical exam for a school," "medical in-processing," OCONUS to CONUS testing, "condition of job" (i.e., testing other than high-risk occupation).
[d]The only reason for confirmatory testing considered valid was to verify an equivocal, invalid, or indeterminate test. Other reasons for confirmatory testing included patient request (n=8), confirm a positive tuberculin skin test (n=28), and history of Bacille Calmette-Guérin vaccination (n=15).

(66%). Of the cases who were prescribed treatment, 74% were given isoniazid; the remaining cases were prescribed rifampin. Of the 62 cases who had liver enzyme tests performed before initiating therapy, 28 (45%) had no indication for testing **(data not shown)**.[14] The treatment index of those with no prior deferral was 81%, which was significantly higher than the 39% seen in those who did have a prior treatment deferral (risk ratio = 2.1 [95% confidence interval: 1.6–2.7]) **(data not shown)**. The median delay in treatment initiation was also 2.5 years longer for prior deferrals: 1,091 versus 196 days (p<0.00001). However, it should be noted that, in 2013, a new U.S. Army regulation aligned the two.[15]

The results of repeat tests are shown in **Table 3**. Repeat tests were typically performed to "confirm" the diagnosis of LTBI. Although 80% of initial testing was performed with TST, 54% of repeat testing was performed with an IGRA (p<0.00001). Testing was repeated in 63 of 171 individuals (37%) with an initially positive TST, but among only two of 44 (5%) of those with an initially positive IGRA (p=0.00001). The proportion of positive repeat tests was generally high (76%) but varied by test type, with 35 of 37 (95%) repeat TSTs positive and 26 of 43 (60%) repeat IGRAs positive (p=0.0005). The mean times between subsequent tests were often long (means of 1.1 to 3.8 years).

Seventeen (8%) service members were not treated as LTBI based on repeat testing and were considered non-counts; an additional two individuals had negative tests but were still treated as LTBI based on clinician judgment. Four (2%) persons were found to not meet the CDC clinical criteria for LTBI based on the initial test and were also classified as non-counts without repeat testing. Treatment data for the remaining 194 cases classified as having LTBI are presented in **Table 4.** The most common reason for treatment non-initiation was provider deferral (77%), whereas the most common reason for non-completion after initiation was patient refusal or non-compliance

TABLE 3. Results of repeat testing for latent tuberculosis infection

	Fort Drum		Fort Benning		TAMC		Total (%)	
Initial test								
TST	74	100%	65	93%	32	45%	171	80%
IGRA	0	0	5	7%	39	55%	44	20%
Repeat testing after positive TST								
Had second test after initial positive	32		13		18		63/171	37%
TST	11	34%	7	54%	10	56%	28	44%
Follow-up TST positive	10/11	91%	7/7	100%	9/10	90%	26/28	93%
IGRA	21	66%	6	46%	8	44%	35	56%
Follow-up IGRA positive	13/21	62%	2/6	33%	6/8	75%	21/35	60%
Mean time between first and second tests [years]	1.4		2		2		1.7	
Had third test after positive TST	3		3		5		11/171	7%
TST	3	100%	2	67%	1	20%	6	55%
Follow-up TST positive	3/3	100%	2/2	100%	1/1	100%	6/6	100%
IGRA	0	0	1	33%	4	80%	5	45%
Follow-up IGRA positive	N/A		1/1	100%	3/4	75%	4/5	80%
Mean time between second and third tests [years]	2.4		1.5		1.5		1.7	
Had fourth test after positive TST	1		1		2		4/171	2%
TST	1	100%	0	0	2	100%	3	75%
Follow-up TST positive	1/1	100%		N/A	2/2	100%	3/3	100%
IGRA	0	0	1	100%	0	0	1	25%
Follow-up IGRA positive	N/A		1/1	100%	NA		1/1	100%
Repeat testing after positive IGRA								
Had second test after positive IGRA	0	0	0	0	2	2	2/44	5%
TST	0	0	0	0	0	0	0	0
IGRA	0	0	0	0	2	2	2	100%
Follow-up IGRA positive	N/A		N/A		0/2	0%	0/2	100%

IGRA=interferon-gamma release assay, TAMC=Tripler Army Medical Center, TST=tuberculin skin test

TABLE 4. Treatment indices[a] for service members with latent tuberculosis infection

	Fort Drum (N = 65)		Fort Benning (N = 63)		TAMC (N = 66)		p-value	Total (N = 194)	
Initiation index[b]	55/65	85%	33/63	52%	58/66	88%	<0.0001	146/194	75%
Reasons for non-initiation									
Provider deferral	6	60%	27	90%	4	50%		37	77%
Patient refusal/non-compliant	4	40%	2	7%	4	50%		10	21%
Unknown	0		1	3%	0			1	2%
Completion index[c]	41/55	75%	32/33	97%	41/58	71%	0.004	114/146	78%
Reasons for non-completion									
Provider deferral	2	14%	0	0	3	18%		5	16%
Patient refusal/non-compliant	9	64%	1/1	100%	11	65%		21	66%
Adverse medication event	1	7%	0	0	1	6%		2	6%
Separated from service	2	14%	0	0	2	12%		4	13%
Treatment index[d]	41/65	63%	32/63	51%	41/66	62%	0.29	114/194	59%

TAMC=Tripler Army Medical Center

[a]Excludes 21 subjects who were found to not have latent tuberculosis infection after evaluation (Fort Drum, n=9; Fort Benning, n=7; TAMC, n=5)

[b]The proportion of all latent tuberculosis infection cases who initiated therapy

[c]The proportion of cases who completed a standard course of therapy among those who initiated therapy

[d]The proportion of all latent tuberculosis infection cases who completed therapy; also, the product of the initiation index and the completion index

substantial delays in treatment were also seen in the no deferral group, largely due to delayed treatment initiation at basic training installations.

Data quality was assessed in **Table 5**. Of the 215 patients, 57 were excluded: 21 were found not to have LTBI, and 36 were discharged from the military and their records were no longer available in the U.S. Army's electronic TB registry (MEDPROS). All cases who had TSTs performed had quantitative readings documented in MEDPROS, but none of those who had IGRAs performed had a quantitative result documented. MEDPROS currently accepts only "positive" or "negative" values for IGRA tests. Overall, 70% of the cases had all of the listed TB testing items complete and correct when excluding quantitative IGRA results, or 42% if these were included **(data not shown)**. The electronic medical record (AHTLA) had quantitative IGRA results available for 31% of the cases who had an IGRA performed.

Table 6 compares LTBI performance indicators with U.S. Army performance targets. Although all patients were eventually evaluated by a provider, only 59% were evaluated within 30 days. Similarly, although 75% of cases initiated LTBI therapy, only 7% did so within 30 days of the initial positive test. The overall treatment index of 59% did not meet the target of 75%. Although testing of high-priority service members was high (probably close to 100%), up to 93% of those testing positive were low-priority individuals.

TABLE 5. Assessment of tuberculosis test registry data quality for latent tuberculosis infection cases

No. of cases in registry[a]	Fort Drum N=49		Fort Benning N=53		TAMC N=56		Total count (%) N=158	
Exemption to further testing was documented	49	100%	42	79%	50	89%	141	89%
TST or IGRA administration was documented	47	96%	47	89%	53	93%	147	93%
Any TST reading was documented	42/46	91%	37/41	90%	27/30	90%	106/117	91%
Quantitative TST reading was documented in millimeters	42	100%	37	100%	27	100%	106	100%
Valid interval was documented for TST reading[b]	40	95%	35	95%	22	81%	97	92%
Quantitative IGRA result was documented	0/13	0%	0/6	0%	0/38	0%	0/57	0%
Test result and exemption both indicate a positive test	43/44	98%	38/46	83%	47/50	94%	128/140	91%
All of the items above were documented correctly.[c]	40/49	82%	33/53	62%	38/56	68%	111/158	70%

IGRA=interferon-gamma release assay, TAMC=Tripler Army Medical Center, TST=tuberculin skin test

[a]Does not equal 215 because of cases found not to have latent tuberculosis infection (n=21) and records no longer maintained after discharge from military service (n=36)

[b]TST read 48–72 hours after administration

[c]Does not include quantitative IGRA result data. If included, the overall proportion decreases from 70% to 42%.

TABLE 6. Comparison of latent tuberculosis infection indicators with U.S. Army performance targets

Indicator	U.S. Army performance target	Measured performance
Proportion of testing performed among those at low risk for infection	≤10%	93%
Evaluation by public health <30 days after positive test	100%	59%
Time to treatment initiation <30 days after initial positive test	≥90%	7%
Treatment index	≥75%	59%
Initiation index	≥85%	75%
Completion index	≥85%	78%
Quantitative IGRA result available	≥95%	
In the electronic medical record		31%
In the electronic tuberculosis test registry		0%
Quantitative TST result available	≥95%	100%
Exempted from further testing after positive test	≥95%	89%

IGRA=interferon-gamma release assay, TST=tuberculin skin test

EDITORIAL COMMENT

This is the first known report detailing the implementation of an LTBI cohort review, although a brief summary of this report is pending publication.[16] Completion of therapy was good (78%) once initiated, but unnecessary delays in treatment initiation occurred due to provider deferral, particularly at time of entry into service. Most tests (93%) were performed among study participants who were at low-risk for TB infection, despite CDC and Department of Defense guidelines discouraging this.[13,17] Most (76%) of the repeat tests, typically performed to "confirm" the diagnosis of LTBI, were positive. These led to average treatment delays of 1.7 years. Deferral led to worse treatment outcomes both in completion of therapy and time to treatment. Despite the availability of an electronic TB registry, data quality did not meet performance targets.

A previous cohort review of TB disease in the U.S. Army revealed that indicators met most of the CDC performance targets.[5] Similar to this study, previous cohort reviews of TB disease have identified programmatic issues in need of improvement in the areas of case management and public health practice.[2] No CDC performance targets have been established for the LTBI cohort review, but national estimates have suggested that less than half of the people starting treatment for LTBI complete therapy.[18] A major reason for this low level is the fact that LTBI treatment is not compulsory. However, this observation also suggests that substantial improvement is possible.

Strengths of this study include the comprehensive nature of this program, the ability to ensure relatively complete follow-up, and the evaluation of the program under real-world conditions. Limitations include a small sample size, small number of sites sampled, and problems with missing or misclassified data. In particular, the proportion of positive repeat testing was higher than expected in light of the known variability of both the TST and IGRA.[19,20] Estimates of agreement between tests could be biased upward if those with positive repeat tests were more likely to have LTBI records available at installation PM services, or if those with a higher likelihood of infection were offered repeat testing with a TST rather than an IGRA. The low TB incidence and unique military exposures of the population studied may further limit the generalizability of this study.

A critical element of TB control and prevention in low-incidence settings is finding and managing cases of LTBI. Important ways of managing LTBI at the installation include ensuring the completeness and effectiveness of contact investigations, maintaining technical skills in TST performance (and IGRA if applicable), and improving the efficiency and effectiveness of targeted testing programs.[3] This cohort review identified several areas that can be targeted as part of a comprehensive program improvement. This study suggests that LTBI program improvement in the U.S. Army should be directed toward reducing testing of low-risk populations, increasing the initiation and completion of LTBI treatment, reducing treatment delays, and ensuring data completeness and accuracy.

Testing of low-risk populations can be reduced by the implementation of targeted testing, which reduces unnecessary testing and improves program efficiency.[13,21] The settings in which most testing was performed are the highest priority for targeted testing implementation, including testing at entry into service and before and after deployment to TB-endemic locations. A 2013 U.S. Army regulation has already put these changes into policy.[15] Confirmatory (repeat) testing was not seen to be particularly useful in this study, because most (76%) of repeat tests were also positive. Additionally, such testing contributes to delays in treatment and treatment failures. This study suggests that elimination of confirmatory testing, or at least reducing it to situations recommended by CDC,[7] is warranted.

This study also suggests that LTBI treatment initiation and completion can be improved. The most common reason for treatment failure was provider deferral of initiation. Provider education, feedback, and program monitoring and evaluation can be used to improve this, particularly at sites that receive soldiers at initial entry into military service. Although LTBI treatment is not compulsory in civilian settings, untreated LTBI is a disqualifying condition for military service.[22] A policy to make LTBI treatment compulsory at time of entry into military service was also introduced in the 2013 regulation.[15] The same interventions can be used to reduce treatment delays.

Finally, data quality can be improved through education and feedback and through program monitoring and evaluation. Informatics tools can be applied

toward LTBI program management, using the information infrastructure to improve the workflow processes, data capture, referrals between installations, and adherence to treatment. These tools could be used to improve program evaluation through surveillance of TB testing and treatment data. An electronic TB registry is already used to document testing and exemptions to further testing in the U.S. Army; this capability could be expanded to the other Services. The TB test registry could also be expanded to include documentation of treatment initiation and completion.

The LTBI cohort review can be a useful tool toward improved TB control in low-incidence populations such as the U.S. military. This report describes a method of operationalizing this type of cohort review. As exemplified by the cohort review for TB disease, program improvement is only achieved through accountability and continued action based on the findings of evaluations of program outcomes. In addition to regular training, education, and assessment, preventive medicine personnel at U.S. military installations should perform a LTBI cohort review at least annually to ensure the quality of the TB control program.

Disclaimer: The material has been reviewed by the Uniformed Services University. There is no objection to its presentation or publication. The opinions or assertions contained herein are the private views of the authors, and are not to be construed as official, or as reflecting true views of the Uniformed Services University, Department of the Army, or the Department of Defense.

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Brief Report

Number of Tuberculosis Tests and Diagnoses of Latent Tuberculosis Infection in Active Component Service Members, U.S. Armed Forces, January 2004–December 2014

Individuals who are infected with *Mycobacterium tuberculosis* (the bacterium that causes tuberculosis) can have either active tuberculosis (TB) or latent TB infection (LTBI). Individuals with LTBI are infected but have no signs or symptoms of TB disease and cannot spread the disease. The diagnosis of latent tuberculosis infection (LTBI) relies on measurement of host immune response through the tuberculin skin test (TST) or interferon-gamma release assays (IGRAs), tests that measure response to TB proteins in blood. An individual who tests positive on these tests should have additional medical evaluation, including a chest x-ray and a sputum test for *M. tuberculosis* bacteria to determine whether he or she has active TB.[1,2]

TB surveillance in U.S. military members has been routinely performed since World War I. A recent review of TB trends in the U.S. Armed Forces reported that the rate of active TB in the U. S. military is lower than that of the U.S. population; however, the same review also reported that the most common factor associated with the diagnosis of active TB during military service was latent infection at time of entry into the military.[3]

This report summarizes the number and trends of TB tests and subsequent LTBI diagnoses in active component military members.

METHODS

The surveillance period was 1 January 2004 through 23 December 2014. The surveillance population included all individuals who were screened for tuberculosis via a TST or IGRA while serving as a member of the active component of the Army, Navy, Air Force, Marine Corps, or Coast Guard at any point during the surveillance period.

For these analyses, the immunization records and electronic records of inpatient or outpatient medical encounters of service members were examined for immunization type codes or Current Procedural Terminology (CPT) codes indicating a TST or IGRA test as listed in **Table 1**. A service member was restricted to having a maximum of one TB test per day. An LTBI diagnosis was defined as having any of the ICD-9 codes listed in **Table 1** entered into any diagnostic position of an inpatient or outpatient medical record, or in a record of a medical encounter in the Theater Medical Data Store (TMDS) within 30 days of a TB test. The data used in this analysis were derived from the Defense Medical Surveillance System (DMSS), which maintains electronic records of all actively serving U.S. military members' hospitalizations and ambulatory healthcare visits in U.S. military and civilian (contracted/purchased care through the Military Health System) medical facilities worldwide and diagnoses associated with deployment documented in the TMDS.

Both the number of total TB tests performed and the number of unique individuals with a record of a TB test were calculated. LTBI percentages were calculated by determining the number of individuals with a TB test as the denominator and the number of LTBI diagnoses as the numerator. For this analysis, a service member had to have a recorded TB test to qualify as a case of LTBI. Service members who had an LTBI diagnosis code only and no record of a TB test in their medical record were excluded from this analysis.

Both the number of tests performed

TABLE 1. Defining ICD-9 and procedure codes for latent tuberculosis infection and tuberculosis testing

Latent tuberculosis infection	
ICD-9 diagnostic codes	
795.5	Nonspecfic reaction to test for tuberculosis
795.51	Nonspecific reaction to tuberculin skin test without active tuberculosis
795.52	Nonspecific reaction to cell mediated immunity measurement of gamma interferon antigen response without active tuberculosis
Immunization type code	
095	Tuberculin skin test, old tuberculin multipuncture device
096	Tuberculin skin test; purified protein derivative solution, intradermal
097	Tuberculin skin test; purified protein derivative solution, multipuncture
098	Tuberculin skin test, NOS
Outpatient Current Procedural Terminology (CPT) codes	
86580	Skin test; tuberculosis, intradermal
86480	Tuberculosis test, cell mediated immunity measurement of gamma interferon antigen response
86481	Tuberculosis test, cell mediated immunity measurement; enumeration of gamma-interferon-producing T-cells in cell suspension
86585	Skin test; tuberculosis, tine test

and the number of LTBI diagnoses were summarized separately for 2014; the data for 2014 are incomplete because the data available for analysis could not include all of 2014 at the time the analysis was performed.

RESULTS

A total of 5,501,349 TB tests were performed on 4,569,791 service members during the course of the surveillance period; 58,118 service members (1.3%) received a diagnosis of LTBI. **(Table 2)** During 2004–2013, the annual percentage of service members tested for TB who received an LTBI diagnosis fluctuated between a low of 0.9 % in 2011 to a high of 1.6% in 2006.

The vast majority of TB tests performed during the surveillance period were TSTs; less than 1% were IGRAs. Approximately 23% of tests were performed in service members during their initial or recruit training periods **(data not shown).**

Throughout the surveillance period, the percentage of Asian/Pacific Islanders who were diagnosed with LTBI was two to five times that of other race/ethnicity groups **(Table 2)**. No other demographic characteristics (e.g., gender, age) were consistently associated with greater prevalence of LTBI diagnosis.

The number of tests performed in 2014 (through 23 December 2014) was 149,531 and the number of service members tested was 135,787; this finding represented a decrease of more than 200,000 tests from the number performed in the prior year. In addition, the percentage of service members receiving an LTBI diagnosis (n=3,361) within 30 days of their test increased to 2.7%. The number of tests performed by the Army declined by 72% between 2013 and 2014; similar declines of lesser magnitude were observed in the Navy (24%), Air Force (27%), and Marine Corps (32%) **(Figure)**.

EDITORIAL COMMENT

More than 5.5 million TB tests were performed in active component service members since 2004; however, during 2004–2013, the overall crude percentage of service members receiving a diagnosis of LTBI within 30 days of a TB test was relatively low (1.3%). The number of TB tests performed was much lower in 2014, compared to prior years; the overall percentage of tested service members receiving an LTBI diagnosis was higher than that during the rest of the surveillance period (2014: 2.7% vs. 2004–2013: 1.3%).

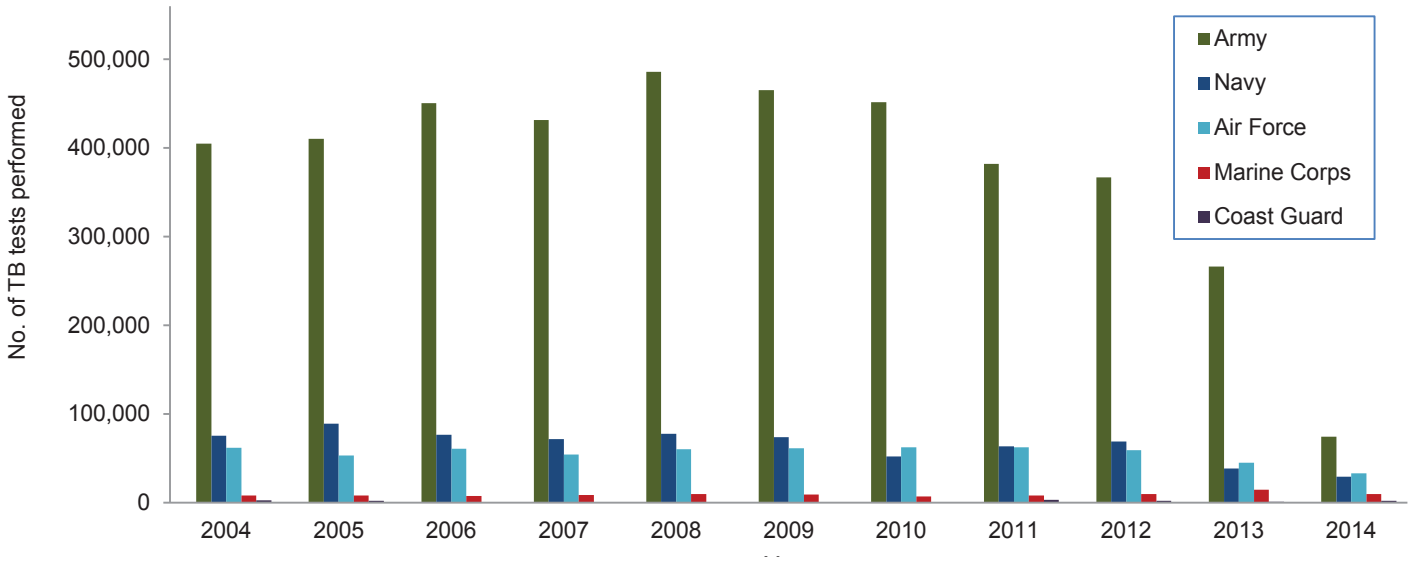
In November 2013, the U.S. Army Medical Command issued a new regulation (MEDCOM Regulation 40-64) for the Tuberculosis Surveillance and Control Program, which recommended that TB testing should be targeted to individuals at high risk and discouraged in those at low risk of TB.[4] It is possible that implementation of this policy might have been responsible for the substantial decline in the number of TB tests performed in 2014. As mentioned in the Methods, the 2014 data are incomplete. However, it is unlikely that a decline of the magnitude reported is the result of the absence of data from the very end of the year. Moreover, if targeted testing of individuals at higher risk of TB was achieved, as recommended in the new Army regulation, this may have contributed to the increase in the percentage of service members receiving an LTBI diagnosis. It would be expected that a similar increase in the percentage of active TB cases might also be observed through employment of a targeted testing strategy; however, this analysis did not attempt to quantify the number of active TB cases in active component service members. Historically, the rate of active TB disease in active component service members has been very low (0.6 per 100,000 population).[3]

As with any analysis utilizing administrative data, there are significant limitations that need to be considered when interpreting these findings. Quantifying the number of TB tests in this population relied on the entry of a specific code indicating a TB test in the immunization record or in a medical record. Therefore, any test administered that

TABLE 2. Numbers of TB tests administered and persons tested, and percentages of tested persons diagnosed with latent tuberculosis infection (LTBI) by race/ethnicity, active component, U.S.

		No. of persons tested, by race/ethnicity						Percentage of + tests for LTBI by race/ethnicity					
Year	Total no. of tests	No. of persons tested	White, non-Hispanic	Black, non-Hispanic	Hispanic	Asian/ Pacific Islander	Other	Overall % with LTBI	White, non-Hispanic % with LTBI	Black, non-Hispanic % with LTBI	Hispanic % with-LTBI	Asian/ Pacific Islander % with LTBI	Other % with LTBI
2004	554,203	456,890	287,938	86,686	45,762	14,853	21,646	1.1	0.7	1.6	1.6	2.9	1.4
2005	563,830	472,212	297,747	85,908	48,957	15,967	23,633	1.5	1.0	2.0	2.2	3.8	1.8
2006	597,700	489,551	311,679	86,391	51,038	16,358	24,085	1.6	1.1	2.3	2.6	4.9	2.2
2007	568,237	465,693	298,632	79,349	49,690	15,704	22,318	1.5	1.0	2.1	2.4	4.5	2.1
2008	635,318	515,196	328,994	88,883	55,680	16,774	24,865	1.4	0.8	2.1	2.1	4.4	2.2
2009	611,529	504,564	321,683	86,894	53,280	16,757	25,950	1.2	0.8	1.9	1.8	4.3	1.9
2010	575,123	479,254	306,016	82,902	50,810	16,572	22,954	1.0	0.6	1.4	1.5	3.7	1.9
2011	520,286	437,241	275,440	75,407	47,928	15,366	23,100	0.9	0.5	1.4	1.3	3.4	1.6
2012	507,752	430,312	267,244	74,872	48,608	15,650	23,938	1.0	0.5	1.6	1.3	3.5	1.4
2013	367,371	318,878	195,811	58,595	36,294	12,994	15,184	1.5	0.9	2.5	2.0	5.2	1.9
Total	5,501,349	4,569,791	2,891,184	805,887	488,047	156,995	227,673	1.3	0.8	1.9	1.9	4.0	1.8

FIGURE. Number of tuberculosis (TB) tests performed by Service by year, 2004–2014[a]



[a]Data through 23 December 2014

was not recorded in this way would not be counted in this analysis and the estimated totals of TB tests would be an underestimation. In addition, the ascertainment of LTBI was solely derived from ICD-9 codes entered into the medical record. Laboratory data (i.e., quantitative or qualitative interpretations of IGRA tests) were not included in this analysis. Additionally, LTBI diagnoses without a corresponding TB test were not included in the counts of LTBI; this may have resulted in an underestimation of the rate of LTBI in the active component population.

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Incidence of *Campylobacter* Infections Among Service Members of the Active and Reserve Components of the U.S. Armed Forces and Among Other Beneficiaries of the Military Health System, 2000–2013

This report reviews the incidence of illness due to *Campylobacter* bacteria based on diagnoses recorded in healthcare records and reported through the Armed Forces reportable medical event (RME) system. During 2000–2013, incident cases of *Campylobacter* infection were diagnosed in 1,393 active component service members, 188 members of the reserve component, and 3,891 retirees and family members. Among members of the active component, incidence rates tended to be higher among females, those aged 40 years or older, members of the Army and Air Force, and officers. Incidence rates declined from 2002 through 2007 but have risen steadily since, especially from 2010 through 2013. Among retirees and family members, the highest numbers of cases were diagnosed among those aged 5 years or younger and those aged 75 years or older. Cases identified through RME reports (n=2,938) showed the highest numbers of cases in May–August, especially July, and that cases reported from Fort Shafter, HI, accounted for 20% of all cases. Measures and precautions important in preventing *Campylobacter* infections as well as other food- and waterborne infections are discussed.

The three species of the bacterial genus *Campylobacter* most often associated with human disease (campylobacteriosis) are *C. jejuni*, *C. fetus*, and *C. coli*.[1] *C. jejuni* in particular is a common cause of gastroenteritis and the Centers for Disease Control and Prevention (CDC) has estimated that *Campylobacter* species represent the third leading bacterial cause of foodborne illness (9% of cases) in the U.S. behind non-typhoidal *Salmonella* (11%) and *Clostridium perfringens* (10%).[2] It is important to note that norovirus is estimated to be the causative agent of 58% of foodborne illnesses. In a study of waterborne disease outbreaks in 2009–2010, the CDC reported that *Campylobacter* was responsible for 12% of such outbreaks but accounted for 78% of the illnesses associated with such outbreaks.[3] Within members of the active component of the U.S. Armed Forces, *Campylobacter* and *Salmonella* are the leading causes of gastrointestinal illness identified in reports of notifiable diseases.[4,5] The Armed Forces Reportable Medical Events Guidelines and Case Definitions require the submission of reports of *Campylobacter* infections, particularly cases of illness due to *C. jejuni*.[6]

The most common presentation of *C. jejuni* illness is gastroenteritis with typical signs and symptoms of diarrhea, fever, malaise, and abdominal pain.[1] Tissue injury occurs in both the small and large intestines and in some cases the diarrhea may be bloody. Depending on the infectious dose of bacteria ingested, the incubation period may vary from 1 to 7 days. When illness affects previously healthy individuals, recovery without specific antibiotic therapy within a week is the rule, but in more severe cases or in persons with other underlying illnesses, antibiotics may be appropriate.[1]

Campylobacter are commonly found in the intestinal tracts of a wide variety of wild and domesticated animals, including cattle, sheep, swine, goats, dogs, cats, rodents, poultry, and other birds. Consumption of undercooked meat, especially poultry, is commonly associated with human infection, but sporadic cases and outbreaks have been linked to unpasteurized milk and other dairy products. Other documented routes of infection include ingestion of contaminated drinking water or immersion in surface water, as well as direct transmission from infected animals and humans.[1,7,8]

This report reviews the incidence of diagnoses of campylobacteriosis in service members and other beneficiaries of the Military Health System (MHS) over the past 14 years.

METHODS

The surveillance period was 1 January 2000 through 31 December 2013. Three separate populations were examined for incident cases of *Campylobacter* infection. The first surveillance population consisted of all active component service members of the U.S. Armed Forces who served at any time during the surveillance period. For this population, the availability of personnel data about time in service and other demographic information enabled the calculation of incidence rates based on person-time in service. The other populations considered separately were members of the reserve component (Reserve and National Guard) and other beneficiaries (retirees and family members) of the MHS. For the latter two populations, data for person-time were not available for calculation of incidence rates, so only counts of cases are described. Diagnoses of *Campylobacter* infection were derived from records of reports of notifiable medical events and from administrative records of all medical encounters of individuals who received care in fixed (i.e., not deployed

or at sea) medical facilities of the MHS or civilian facilities in the purchased care system. All such records are maintained in the electronic records of Defense Medical Surveillance System (DMSS). For surveillance purposes, an incident case of *Campylobacter* infection was defined on the basis of a reportable medical event (RME) record of "confirmed" *Campylobacter* infection or a record of one inpatient or one outpatient encounter documented with the requisite ICD-9-CM code (008.43) in any diagnostic position. An individual could be considered a case once every 180 days. Individuals whose *Campylobacter* infection was identified in more than one type of record were de-duplicated by counting cases according to the descending priority of RME report, inpatient record, and outpatient record. For example, an individual who had inpatient and outpatient encounters and an RME report for campylobacteriosis within a 180-day period would be categorized as having been identified via the RME system.

TABLE 1. Incident cases and rates of *Campylobacter* infection, active and reserve components, U.S. Armed Forces, 2000–2013

	Active component		Reserve component
	No. of cases	Rate[a]	No. of cases
Total	1,393	0.70	188
Sex			
Male	1,157	0.68	157
Female	236	0.81	31
Age group			
<20	88	0.33	6
20–24	347	0.66	27
25–29	373	0.84	30
30–34	217	0.73	25
35–39	171	0.69	38
40–44	123	0.86	29
45–49	47	0.91	21
50+	27	1.56	12
Race/ethnicity			
White, non-Hispanic	961	0.77	153
Black, non-Hispanic	134	0.39	10
Hispanic	144	0.70	12
Other	154	0.77	13
Service			
Army	640	0.89	116
Navy	224	0.46	12
Air Force	427	0.89	53
Marine Corps	78	0.30	6
Coast Guard	24	0.43	1
Rank			
E01–E04	497	0.57	46
E05–E09	550	0.69	88
O01–O04	257	1.06	31
O05–O11	68	1.15	18
W01–W05	21	0.80	5

[a]Cases per 10,000 person-years

RESULTS

Active component

During the 14-year surveillance period, there were 1,393 incident cases of *Campylobacter* infection in active component members. The overall incidence rate was 0.70 cases per 10,000 person-years (p-yrs). The numbers of cases, overall incidence rates, and distribution by various demographic characteristics are shown in **Table 1**. Compared to their respective counterparts, the overall incidence rates of *Campylobacter* infection were higher in female service members, those aged 40 years or older, members of the Army and Air Force, and officers. Rates were lowest among black, non-Hispanic service members compared to the other racial/ethnicity groups **(Table 1)**. It is noteworthy that the numbers and annual incidence rates of cases of *Campylobacter* infection declined from 2002 (rate of 0.70 per 10,000 p-yrs) through 2007 (rate of 0.39 per 10,000 p-yrs), but thereafter increased, and rose especially sharply from 2010 (rate of 0.69 per 10,000 p-yrs) through 2013 (rate of 1.39 per 10,000 p-yrs) **(Figure 1)**. Annual incidence rates increased among all of the demographic categories from 2007 through 2013.

Reserve component

A total of 188 incident cases of *Campylobacter* infection were identified among members of the reserve component during the 14-year surveillance period **(Table 1)**. Because it was not possible to calculate incidence rates for this population, the distribution of diagnoses by demographic characteristics cannot be readily compared to the distribution among members of the active component. However, the preponderance of cases among members of the reserve component occurred among white, non-Hispanics (81%) and members of the Army (62%) and Air Force (28%). The temporal trend in annual numbers of cases resembled that for the active component, with 107 (57%) of cases occurring during the past 5 years **(Figure 2)**.

Other beneficiaries

The population of other beneficiaries differs considerably from that of service members (both active and reserve components) with respect to several demographic characteristics. Notably, there are many more "other beneficiaries" (7.3 million, of

whom at least 5.3 million are enrolled in TRICARE) than there are service members (2.3 million).[9] Moreover, there are many aged 17 years or younger, many aged 60 years or older, and a much greater proportion of females than is the case with service members. During the surveillance period, there were 3,891 incident cases of *Campylobacter* infection among other beneficiaries **(Table 2)**. Cases among females (n=2,117) accounted for 54% of all cases. The age groups with the largest numbers of cases were the youngest and the oldest **(Table 2, Figure 3)**. As was the case with active component service members, the annual numbers of cases rose steeply after 2009 **(Figure 4)**. The youngest and oldest age groups together contributed about 29% of the cases during the past 4 years, proportions similar to their contributions in earlier years **(data not shown)**.

TABLE 2. Incident cases of *Campylobacter* infection, other Military Health System beneficiaries, 2000–2013

	No. of cases	% total
Total	3,891	
Male	1,774	45.6%
Female	2,117	54.4%
Age		
0–4	591	15.2%
5–9	185	4.8%
10–14	132	3.4%
15–19	175	4.5%
20–24	209	5.4%
25–29	153	3.9%
30–34	138	3.5%
35–39	135	3.5%
40–44	185	4.8%
45–49	218	5.6%
50–54	243	6.2%
55–59	247	6.3%
60–64	264	6.8%
65–69	244	6.3%
70–74	232	6.0%
75+	540	13.9%

Seasonality

The 2,938 reports of RMEs of campylobacteriosis among service members and all other beneficiaries were examined to determine the distribution of reported cases by month **(Figure 5)**. The numbers of reported cases during 2000–2013 tended to be highest during May–August, especially July. The lowest aggregate counts were reported in December and February.

Geographic distribution

Of the 145 different medical facilities that submitted RME reports of campylobacteriosis during 2000–2013, 11 facilities submitted more than 50 such reports, accounting for 1,671 cases or 57% of all RMEs for this infection. Fort Shafter, HI, alone submitted 578 case reports, approximately 20% of the total **(Table 3)**. Fort Shafter reported the most cases of any facility every year during the period except for 2004, when its 20 reported cases, its lowest annual number of the entire 14-year period, were exceeded by 21 cases reported by Incirlik Air Base, Turkey. An additional 20 medical facilities reported between 21 and 50 cases during the entire period, accounting for an additional 623 cases (21% of the total) **(data not shown)**.

EDITORIAL COMMENT

Among active component service members of the Armed Forces, the overall incidence rate of campylobacteriosis was 0.70 cases per 10,000 p-yrs and the peak annual incidence rate was 1.39 cases per 10,000 p-yrs in 2013. For many years, the incidence of *Campylobacter* infections in the U.S. exceeded that of *Salmonella*, but a dramatic decline in the former took place between 1996 and 2005, leaving *Salmonella* incidence as the highest among bacterial pathogens. The CDC estimated that the rate of diagnosed cases of *Campylobacter* in the U.S. is approximately 14 per 100,000 population in recent years, but those rates reflect a modest increase from 2006–2008.[10] Similarly, rates in the active component of the Armed Forces have risen steadily from a nadir in 2007. That trend seems to be reflected in the case counts of *Campylobacter* infection for the reserve component and for other beneficiaries

FIGURE 1. Annual numbers of incident cases and incidence rates of *Campylobacter* infection, active component, U.S. Armed Forces, 2000–2013

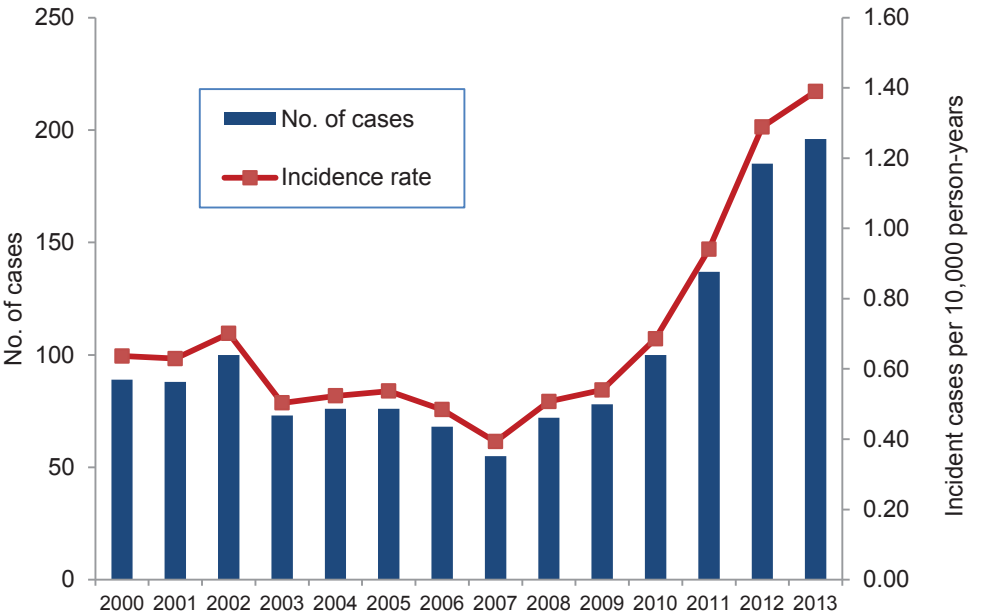


TABLE 3. Sites that most frequently reported cases of *Campylobacter* infection, 2000–2013

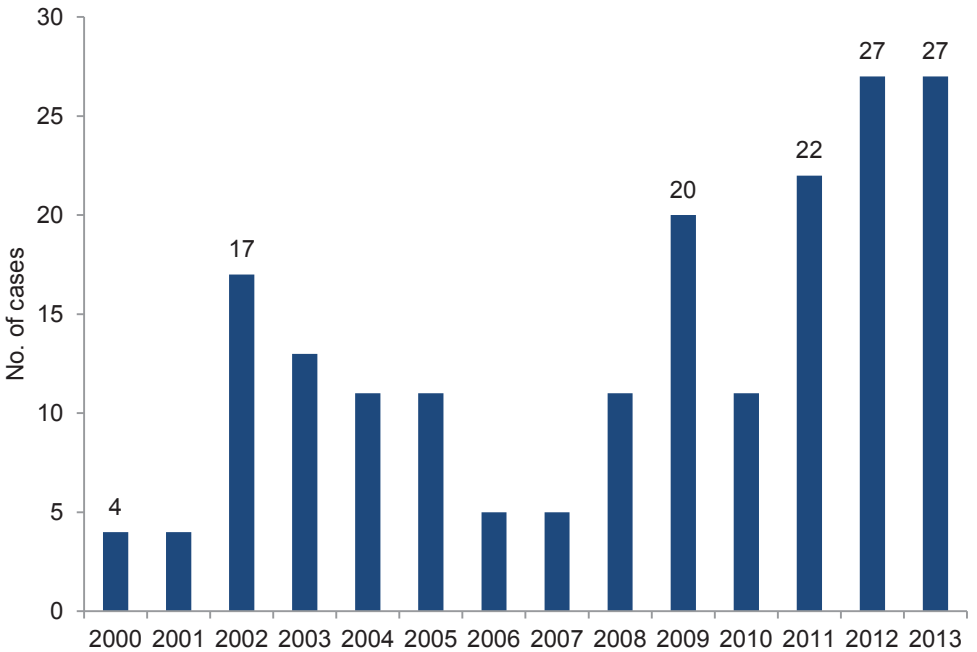
Site	No. of RME cases	% total
Fort Shafter, HI	578	19.7%
Fort Bragg, NC	203	6.9%
Heidelberg, GY	152	5.2%
Fort Belvoir, VA	134	4.6%
Fort Hood, TX	108	3.7%
Joint Base San Antonio, TX	99	3.4%
Fort Carson, CO	89	3.0%
Landstuhl, GY	84	2.9%
Incirlik AB, Turkey	78	2.7%
Joint Base Lewis-McChord, WA	74	2.5%
Pensacola NAS, FL	72	2.5%
All 134 other sites (≤50 cases)	1,267	43.1%
Total	2,938	100.0%

RME=reportable medical event

during the surveillance period. Possible reasons for the observed trend include a true increase in incidence of *Campylobacter* disease associated with a variety of factors, an increase in the frequency with which clinicians order specific diagnostic tests for patients with gastroenteritis, and the increasing laboratory use of "culture-independent diagnostic tests" that may be more sensitive detectors of *Campylobacter* infection.[10]

The modest number (188) of cases identified among members of the reserve component reflects the fact that, on average, their periods of active service during which they are eligible for military health care are limited. It is probable that most of their risk for *Campylobacter* infection, and any associated healthcare encounters, would be related to their lives in the civilian sector.

FIGURE 2. Annual numbers of incident cases of *Campylobacter* infection, reserve component, U.S. Armed Forces, 2000–2013



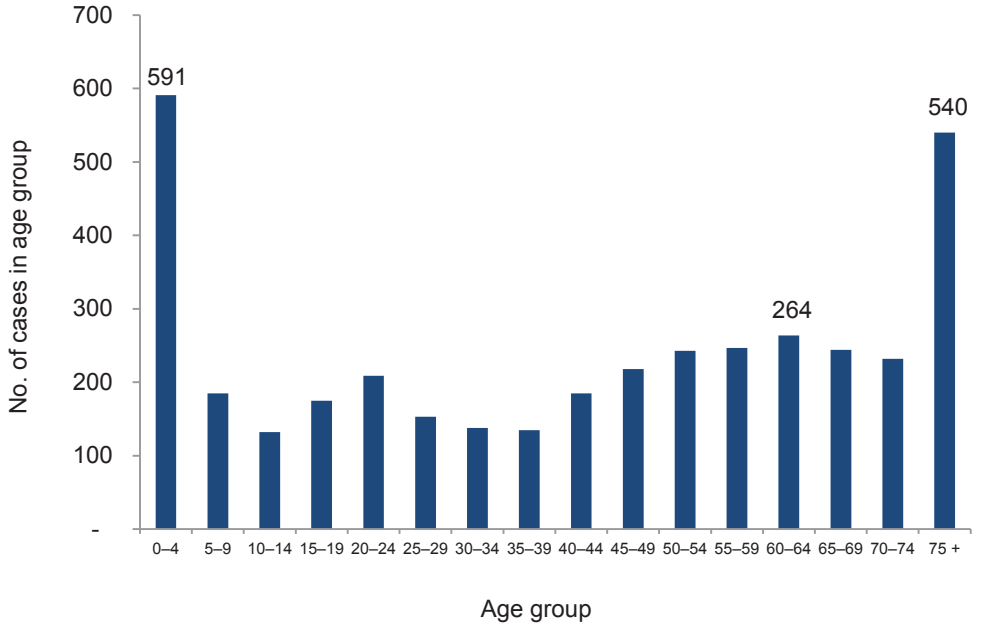
The data on *Campylobacter* illness among "other beneficiaries" reveal a pattern recognized in the general U.S. population. The numbers of cases were dramatically higher among those aged 5 years or younger, as is the case in the U.S. and Europe and also in developing countries.[1] It is unclear whether the large number of cases in the oldest age groups of other beneficiaries reflects increased incidence, increased susceptibility to infection due to changes in host resistance, increased tendency to seek health care with advancing age, or simply a larger population.

The increased numbers of reported cases of campylobacteriosis in the warmest months of the year is consistent with previous studies of the epidemiology of this infection. This seasonality is not well understood. It is possible that some of the risk factors for this infection may relate to warmer weather. For example, human exposure to contaminated water or animals may be greater in warm weather. Transmission by flies, presumably to food or water, has been suggested as a factor of greater import during higher temperatures.[1]

The data on the geographic distribution of military sites reporting *Campylobacter* infections is most striking for the consistently high numbers of cases reported from Hawaii. It has been reported that Hawaii has the highest rates of this infection in the U.S. One study suggests a possible link to consumption of commercially prepared chicken and prior antibiotic use by the victims, but the reasons for this increased incidence remain unclear.[11]

The data in this report indicate that illness due to *Campylobacter* bacteria is relatively common among beneficiaries of the MHS, including service members, family members, and retirees. Following an apparent decline in incidence during the previous decade, the incidence rate among active component service members and

FIGURE 3. Age distribution of incident cases of *Campylobacter* infection among other Military Health System beneficiaries, 2000–2013



case counts among all beneficiaries during the past 4 years indicate that preventive measures must be routinely emphasized. Sporadic cases have been linked to consumption of undercooked meat, especially poultry, as well as contamination of other foods that are served raw, such as salads.[7] As a general rule, meats should be cooked to temperatures (165˚F) that kill the bacteria, and food preparation surfaces and instruments used in preparation of raw meat for cooking should be considered potentially contaminated with *Campylobacter*.[12] Accordingly, either meat should be prepared using separate surfaces (e.g., cutting boards) and utensils, or such objects should be thoroughly cleaned with soap and hot water before use with other foods. CDC guidelines suggest that just one drop of juice from raw chicken meat may contain enough bacteria to cause illness.[7]

Other commonly implicated sources of infectious *Campylobacter* are unpasteurized milk and drinking water, particularly surface water, which has been contaminated by feces from livestock, poultry, or wild birds, but has not been treated adequately with chlorination.[3,8,13,14]

Besides the above precautions, CDC guidelines for preventing *Campylobacter* infection include other measures such as hand washing before and after preparing food, especially raw meats, and after contact with pet feces.[7] All of the above measures are important considerations in the prevention of not only *Campylobacter* disease, but also many other food and waterborne infectious illnesses, including those caused by norovirus, *Salmonella*, *Shigella*, *Escherichia coli*, *Vibrio*, *Yersinia*, and *Clostridium*.

FIGURE 4. Annual numbers of incident cases of *Campylobacter* infection among other Military Health System beneficiaries, 2000–2013

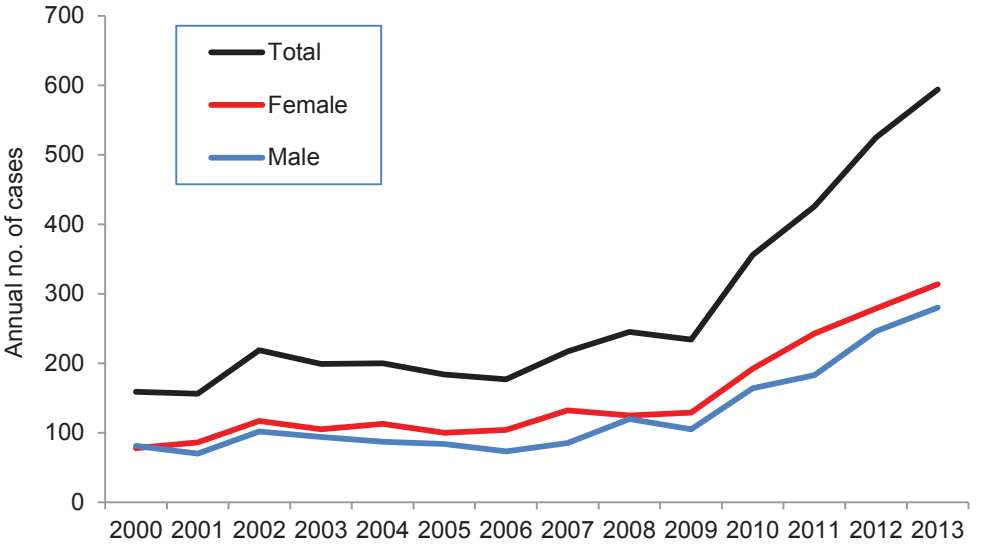


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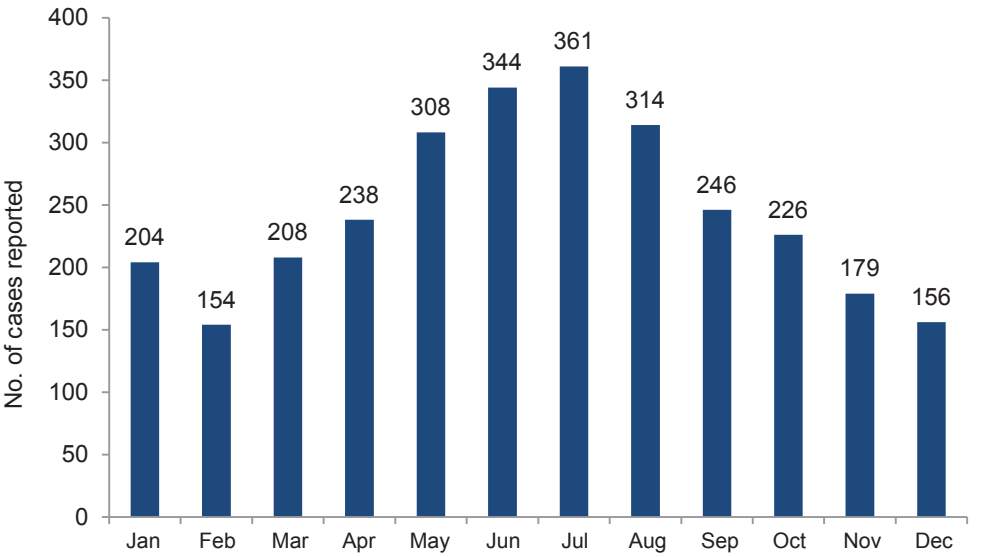
FIGURE 5. Reported cases of *Campylobacter* infection, by month of report, beneficiaries, Military Health System, 2000–2013



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Glaucoma, Active Component, U.S. Armed Forces, 1998–2013

Lee Hurt, DrPH

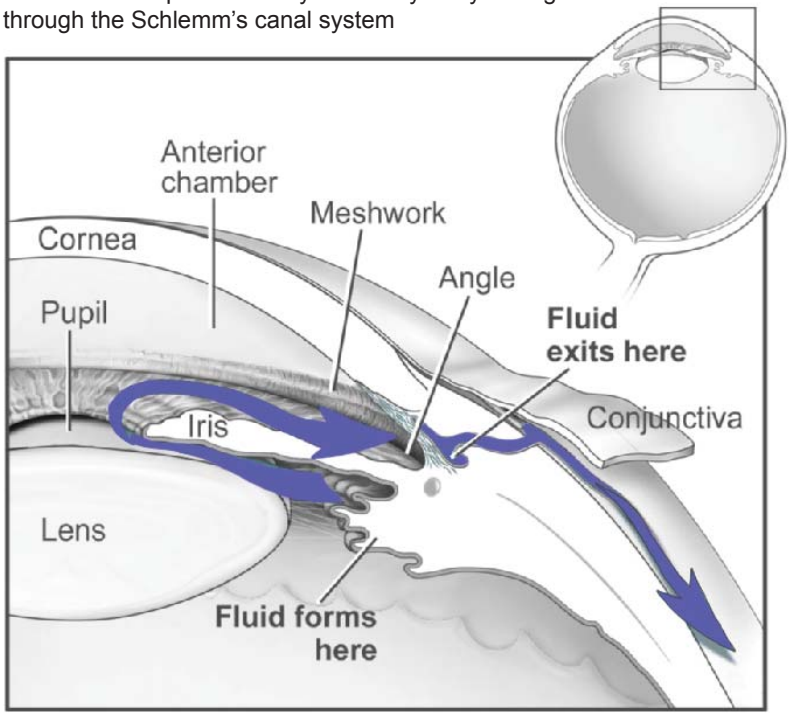
Glaucoma is an eye disease that involves progressive optic nerve damage and vision loss, leading to blindness if undetected or untreated. This report describes an analysis using the Defense Medical Surveillance System (DMSS) to identify all active component service members with an incident diagnosis of glaucoma during 1998–2013. The analysis identified 117,075 incident cases of glaucoma and an overall incidence rate of 5.3 per 1,000 person-years (p-yrs). The majority of cases (94.5%) were diagnosed at an early stage as borderline glaucoma. Over the study period, 5.9% of incident case service members were eventually diagnosed with open-angle glaucoma. There were 26 cases of absolute glaucoma, or total blindness. Rates of glaucoma were higher among black, non-Hispanic (8.8 per 1,000 p-yrs), Asian (6.6), and Hispanic (5.4) service members, compared with white, non-Hispanic (4.2) service members. Rates among female service members (6.0 per 1,000 p-yrs) were higher than those among male service members (5.1). Between 1998 and 2013, incidence rates of glaucoma declined by 48% among service members older than 44 years of age, while rates increased slightly among service members younger than 30 years of age.

Glaucoma is an eye condition that involves optic nerve damage, which in turn, results in loss of vision. This condition is often, but not always, associated with elevated intraocular pressure (IOP). Elevated IOP can be the result of excessive production of aqueous humor, or reduced flow of fluid out of the eye, or both. Aqueous humor is a transparent fluid that fills the anterior and posterior chambers of the eye and flows passively out of the eye **(Figure 1)**. This elevated pressure is believed to result in optic nerve damage in most individuals.[1] Usually, damage to the optic nerve and loss of visual field are gradual and painless; however, there is a form of the disease called acute angle closure, in which the trabecular meshwork becomes blocked, suddenly leading to a rapid rise in IOP and eye pain. This urgent condition requires immediate treatment.[2]

The most common form of glaucoma is open-angle glaucoma. In this form, the drainage area between the cornea and the iris, which forms an angle, is open, but aqueous fluid flow is inadequate. In angle-closure glaucoma, the angle is reduced or blocked by the iris. Other, less common forms of the disease include steroid-induced glaucoma, and those associated with developmental anomalies and systemic syndromes. There are also congenital forms of the disease that are diagnosed at birth or in early childhood.[1] The end stage of the disease, absolute glaucoma, is total blindness.

Risk factors for the development of glaucoma include elevated IOP, 60 years of age or older, black, Asian, or Hispanic race/ethnicity, and a family history of glaucoma.[3,4] Comorbid conditions associated with increased risk for glaucoma include hypertension, diabetes, uveitis, eye injuries, and eye conditions requiring extended corticosteroid use.[5]

FIGURE 1. Cross section of the anterior segment of the eye showing the normal flow of aqueous fluid from its production by the ciliary body through the trabecular meshwork and exiting through the Schlemm's canal system



National Eye Institute, National Institutes of Health

TABLE 1. Diagnostic and procedure codes used for glaucoma classification

Diagnosis classification	ICD-9-CM codes
Congenital/childhood glaucoma	743.2x, 365.14
Borderline glaucoma (glaucoma suspect)	365.0x
Glaucoma unspecified	365, 365.9
Open-angle glaucoma	365.1x
Angle-closure glaucoma	365.2x
Corticosteroid-induced glaucoma	365.3x
Glaucoma associated with anomalies and syndromes	365.4x, 365.5x, 365.6x, 365.8x
Absolute glaucoma	360.42
Screening codes	**ICD-9-CM codes**
Family history of glaucoma	V19.11
Problems with sight	V41.0
Other eye problems	V41.1
Examination of eyes and vision	V72.0
Special screening for glaucoma	V80.1
Procedure classification	**CPT codes**
Eye exam	92004, 92012, 92014
Visual field test	92081, 92082, 92083
Gonioscopy	92020
Serial tonometry	92100
Corneal pachymetry	76514
Opthalmic imaging	92135, 92235

TABLE 2. ICD-9-CM codes used for comorbid conditions

Comorbid condition	ICD-9-CM codes
Diabetes	250.x
Hypertension	401.x, 416.0, 459.3x, 997.91
Cataract	366.x
Uveitis	360.11, 364.3
Eye injury	870.3, 870.4, 871.x, 921.2, 921.3, 921.9

Glaucoma is considered a disqualifying condition for enlistment in the military.[6] Glaucoma that is diagnosed while in service but deemed resistant to treatment or that affects the visual field will be evaluated by a medical examination board for possible separation from service.[6] The condition ranked 69th in the list of diseases and injuries affecting service members, affecting 7,658 service members in 2013.[7]

METHODS

The Defense Medical Surveillance System (DMSS) was used to identify all active component service personnel (Army, Navy, Air Force, Marines, and Coast Guard) whose healthcare records contained a diagnosis of glaucoma during 1 January 1998 through 31 December 2013. The DMSS contains administrative records for all medical encounters of military service members who are hospitalized or receive ambulatory care at military treatment facilities or through civilian purchased care. A case of glaucoma was defined as any active component service member having at least one inpatient, outpatient, or theater medical encounter with a diagnosis of glaucoma **(Table 1)** in any diagnostic position. For each individual who met the case definition, the date of the incident case was defined to be the date of the earliest recorded diagnosis of glaucoma. An individual was counted as an incident case only once during the study period. Service members with incident diagnoses prior to 1998, or with an incident diagnosis while in the Reserve or Guard components were excluded. Medical encounters that included an ICD-9-CM V code for family history of glaucoma or for vision screening were also captured **(Table 1)**. Procedures recommended for the detection and management of glaucoma were identified through the Common Procedural Terminology (CPT) codes shown in **Table 1**.[3,8] These ICD-9 and CPT codes were captured to assess the types of vision screening being performed among service

TABLE 3. Incident counts and rates of glaucoma by demographic and military characteristics, active component, U.S. Armed Forces, 1998–2013

	No.	Rate[a]
Total	117,750	5.2
Sex		
Male	97,715	5.1
Female	19,360	6.0
Race/ethnicity		
White, non-Hispanic	58,814	4.2
Black, non-Hispanic	33,368	8.8
Hispanic	12,096	5.4
Asian/Pacific Islander	5,647	6.6
American Indian/ Alaskan Native	581	2.2
Other/unknown	6,569	6.1
Age group		
<20	4,774	2.9
20–24	26,675	3.6
25–29	22,016	4.5
30–34	16,934	5.1
35–39	19,068	6.8
40–44	16,518	10.8
≥45	11,090	15.6
Service		
Army	43,280	5.4
Navy	27,596	5.1
Marine Corps	10,229	3.5
Air Force	32,919	6.1
Coast Guard	3,051	5.0
Grade		
Junior enlisted	38,139	3.8
Senior enlisted	54,503	6.2
Junior officer	11,480	5.1
Senior officer	12,953	9.4
Occupation		
Combat-related	10,855	3.9
Armor/motor transport	4,670	4.8
Pilot/air crew	3,769	4.5
Repair/engineering	31,853	4.9
Communications/ intel	30,386	6.1
Health care	13,973	7.7
Other	21,569	5.0

[a]Cases per 1,000 person-years

TABLE 4. Counts and percentages of incident diagnoses of glaucoma and of most severe (or specific) diagnoses, by category, active component, U.S. Armed Forces, 1998–2013

	Incident diagnosis category		Most severe (or specific) diagnosis category[a]		% change
	No.	% of total	No.	% of total	
Congenital/childhood glaucoma	54	0.0	42	0.0	-22.2
Borderline glaucoma	110,598	94.5	105,063	89.7	-5.0
Glaucoma unspecified	1,789	1.5	2,514	2.1	40.5
Open-angle glaucoma	3,361	2.9	6,916	5.9	105.8
Angle-closure glaucoma	328	0.3	580	0.5	76.8
Corticosteroid-induced glaucoma	181	0.2	285	0.2	57.5
Glaucoma associated with anomalies, disorders	754	0.6	1,649	1.4	118.7
Absolute glaucoma	10	0.0	26	0.0	160.0
All types	117,075		117,075		

[a]Among all medical encounters with a diagnosis of glaucoma for each service member

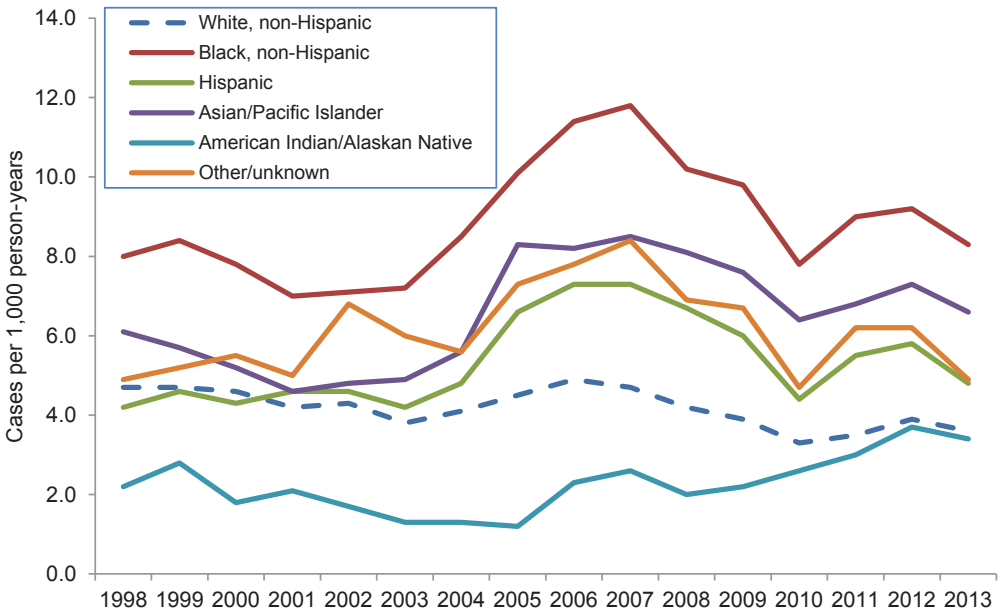
members who were ultimately diagnosed with glaucoma.

In addition to estimating the incidence of glaucoma, the overall burden of glaucoma was measured by counting the number of medical encounters by diagnosis category. Comorbid conditions associated with increased risk for glaucoma were identified, also. These conditions were defined as a single diagnosis, in any diagnostic position, of diabetes, hypertension, cataracts, uveitis, or eye injuries **(Table 2)**, that occurred prior to the incident diagnosis of glaucoma.

Disease progression was analyzed by evaluating changes in diagnosis code categories, and through the use of glaucoma stage ICD-9 codes (365.7x), over time for each service member. Disease progression was estimated to have occurred if an incident diagnosis of glaucoma for the categories of borderline, congenital, or unspecified was followed by a medical encounter with a diagnosis that was more specific or severe than the initial diagnosis (e.g., open-angle, angle-closure, absolute). The possible impact of glaucoma to service career, as measured by time to separation or death, was evaluated.

Denominators for incidence rates of glaucoma were calculated based on the total active component person-time in years for each year in the study period, with time for service members with glaucoma censored at the point of incident diagnosis.

FIGURE 2. Incidence rates of glaucoma by race/ethnicity, active component, U.S. Armed Forces, 1998–2013



RESULTS

There were a total of 117,075 incident cases of glaucoma identified for the period between 1998 and 2013. This represents an overall incidence rate of 5.2 per 1,000 person-years (p-yrs) **(Table 3)**. The rate of glaucoma among female service members was 17.6% higher than that of male service members. The rate was highest among black, non-Hispanic service members (8.8 per 1,000 p-yrs) and it was more than double the rate among white, non-Hispanic service members (4.2 per 1,000 p-yrs). Rates among both Asian and Hispanic service members were also elevated in comparison with white, non-Hispanic service members. As **Figure 2** shows, these disparities were observed across the study period, with the exception of the early period between 1998 and 2000 when the incidence of glaucoma among Hispanic service members was slightly lower than that among

TABLE 5. Number of glaucoma-related encounters associated with the most severe (or specific) diagnoses for service members diagnosed with glaucoma, active component, U.S. Armed Forces, 1998–2013

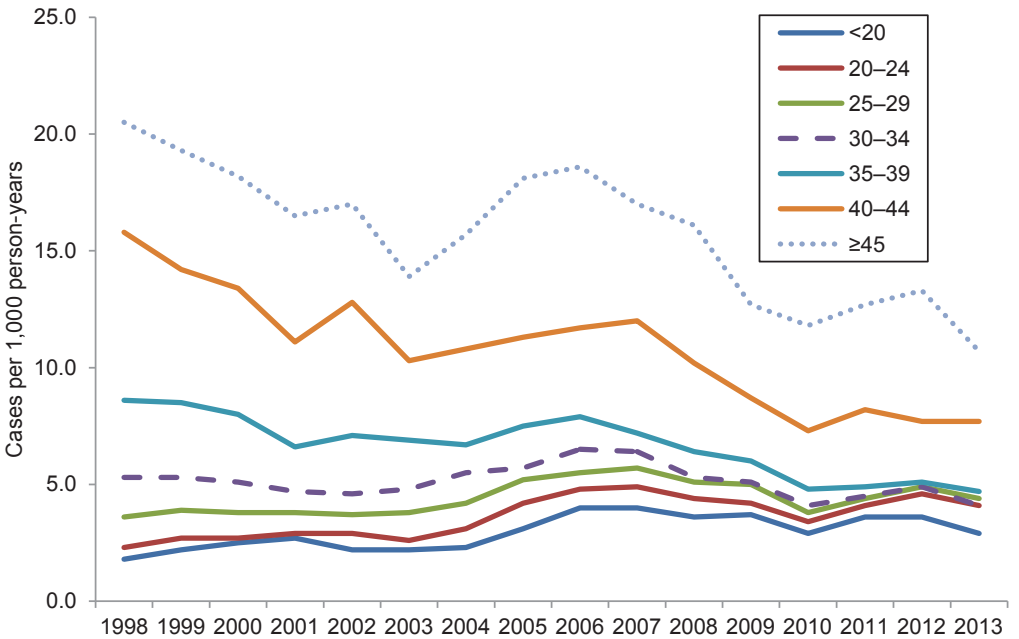
Most severe/specific diagnosis	Medical encounters	
	No.	% of total
Congenital/childhood glaucoma	113	0.0
Borderline glaucoma	352,989	76.7
Glaucoma unspecified	14,335	3.1
Open-angle glaucoma	62,171	13.5
Angle-closure glaucoma	5,665	1.2
Corticosteroid-induced glaucoma	2,022	0.4
Glaucoma associated with anomalies, disorders	22,536	4.9
Absolute glaucoma	524	0.1
All types	460,355	

white, non-Hispanic service members.

The incidence rate of glaucoma increased monotonically with age **(Table 3)**. When viewed over time, rates among service members aged 35 years or older have decreased over time, with the largest declines occurring in those aged 40 years or older **(Figure 3)**. The rate in 1998 among service members aged 45 years or older was 20.5 per 1,000 p-yrs, declining 47.8% by 2013 to a rate of 10.7 per 1,000 p-yrs. Glaucoma rates among service members younger than 30 years of age increased slightly over the study period.

The incidence rate of glaucoma was highest among Air Force personnel (6.1 per 1,000 p-yrs) and lowest among Marines (3.5 per 1,000 p-yrs) **(Table 3)**. Junior-grade service members had lower rates than senior-ranking service members. Rates were higher among officers compared to enlisted personnel. When stratified by occupational category, service members working in the fields of healthcare and communications/intelligence had higher rates of glaucoma than those working in other fields.

FIGURE 3. Incidence rates of glaucoma by age (years) at time of incident diagnosis, active component, U.S. Armed Forces, 1998–2013



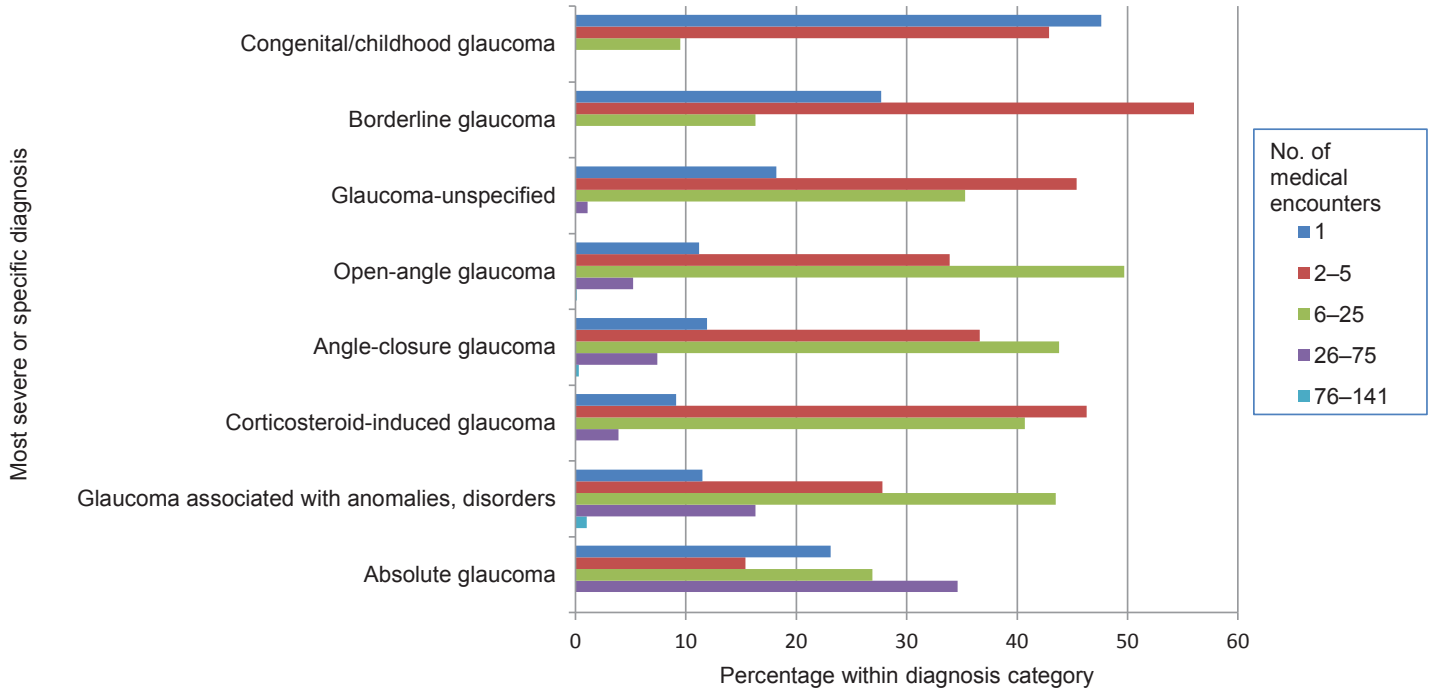
Diagnosis categories and disease progression

When the incident diagnoses were grouped by disease type, 94.5% of the cases were classified as borderline glaucoma **(Table 4)**. The next largest category was open-angle glaucoma, which represented 2.9% of the cases. One and a half percent of the incident cases were coded as glaucoma unspecified, and the other types each represented less than 1% of the total. Of those service members with an initial diagnosis of borderline glaucoma, 3.1% later received a diagnosis of open-angle glaucoma and another 0.8% received other more severe glaucoma diagnoses; however, the majority (95.3%) of these cases did not progress to a more severe stage of the disease during the study period. A total of 5.9% of the incident cases were eventually diagnosed with open-angle glaucoma, 0.5% as angle-closure glaucoma, and 1.4% as glaucoma associated with other disorders. There were a total of 26 service members diagnosed with absolute glaucoma during the study period. Only 0.4% of medical encounters contained disease staging ICD-9 codes (365.7x), so these data were considered too incomplete to rely on for analysis of disease progression.

Burden

The burden of glaucoma was estimated as the number of medical encounters with any glaucoma diagnosis. Among 117,075 diagnosed cases, there were 460,355 such medical encounters. **Table 5** shows the number and percentage of medical encounters when categorized by the most specific or severe diagnosis for each service member over the study period. Even though borderline glaucoma represented 89.7% of the most specific/severe cases, it represented only 76.7% of total medical encounters. The 5.9% of service members ultimately diagnosed with open-angle glaucoma utilized 13.5% of total medical encounters. **Figure 4** shows the patterns of healthcare utilization according to the most severe or specific diagnosis. Among service members

FIGURE 4. Distribution of numbers of glaucoma-related encounters according to the most severe or specific diagnosis category, active component, U.S. Armed Forces, 1998–2013



diagnosed with glaucoma associated with various anomalies or systemic disorders, 16.3% had more than 25 glaucoma-related encounters, and 1.0% had more than 75 encounters. Among those ultimately diagnosed with absolute glaucoma, 34.6% had more than 25 related medical encounters.

Comorbidities

Twelve percent of all service members diagnosed with glaucoma had previously been diagnosed with hypertension. The prevalence of hypertension was highest among those with an incident diagnosis of absolute glaucoma (30.0%), and among those with angle-closure glaucoma (14.0%). High prevalence of prior eye injuries was identified among those with absolute glaucoma (30.0%) and glaucoma associated with other disorders (18.4%). Previous diagnosis of cataracts was higher among those with an incident diagnosis of absolute glaucoma (30.0%), glaucoma associated with anomalies and other disorders (13.5%), and among those with congenital glaucoma (11.1%). Pre-existing uveitis was more common among those with glaucoma associated with other disorders (11.4%) and in those with angle-closure glaucoma (8.2%). Those with absolute glaucoma had the highest prevalence of diabetes (20.0%), followed by those with open-angle glaucoma (3.5%) **(data not shown)**.

Screening and procedures

Of the 117,075 incident cases of glaucoma, 40% had a medical encounter that included a screening code listed in **Table 1**, prior to or at the time of diagnosis. When the analysis was expanded to all medical encounters during the study period for service members with a diagnosis of glaucoma, a total of 138 service members were identified as having a family history of glaucoma.

When the encounters were examined for procedures performed, as documented via CPT codes **(Table 1)**, 86.5% of glaucoma cases had at least one comprehensive eye exam, 65.7% had at least one visual field test, 27.1 % had at least one corneal pachymetry procedure (measuring cornea thickness), 19.5% had ophthalmic imaging performed, 14.3% had documentation of receiving serial tonometry (measuring IOP), and 10.9% had a gonioscopy test to examine the drainage angle **(data not shown)**.

Career impact

The average time to separation or death among service members diagnosed with glaucoma did not vary much when analyzed by the most severe or specific diagnosis received over the study period. On average, the shortest amount of time served following the initial diagnosis with any type of glaucoma occurred among those ultimately diagnosed with corticosteriod-induced glaucoma (3.4 years), followed closely by those diagnosed with absolute glaucoma (3.5 years). The longest serving service members were those with a diagnosis of borderline glaucoma (4.4 years) **(data not shown)**.

EDITORIAL COMMENT

The results of this analysis indicate that most service members (94%) initially diagnosed with glaucoma are in the early stages of the disease (borderline or suspect glaucoma) with indications of elevated IOP but no evidence of optic nerve damage or visual field loss **(Table 4)**. This observation may reflect a transient elevation in IOP, which may never result in nerve damage. Most types of glaucoma progress slowly and can be managed well with medication to reduce aqueous fluid production or increase fluid outflow. Eventually, some cases may require surgery to enable better fluid drainage.[2] Among service members whose disease progressed beyond the borderline diagnosis, prior to separation from service or the end of the study period, the most common form of glaucoma was open-angle, the most frequent type in the general population.[9]

The incidence rate of glaucoma increases with age **(Table 3)**; however, **Figure 3** indicates that rates have decreased over the study period between 1998 and 2013 among older age groups. Rates during the same period increased among the youngest age groups. These findings may reflect improved detection of borderline glaucoma among younger service members. Incidence rates by service were lowest among Marines, which may reflect the younger age distribution of this service. Rates by grade were also lower among junior enlisted and officer service members, again probably due to younger age. Rates by occupational category at incident diagnosis were highest among healthcare workers, possibly due to increased healthcare-seeking behaviors in this group.

Just as in the civilian population, incidence of glaucoma was higher among black, non-Hispanic; Asian; and Hispanic service members compared with white, non-Hispanic or Native American service members **(Table 3)**.[3,4] When the rates by race/ethnicity were displayed over time **(Figure 2)**, most rates peaked in 2007. There was no known change in policy or programs that would have accounted for the increased rate of incident diagnoses around 2007.

Hypertension was an important preexisting condition among those diagnosed with glaucoma. Over 10% of those diagnosed with any type of glaucoma (except congenital) had previously received a diagnosis of hypertension. Thirty percent of those with absolute glaucoma had hypertension. These estimates contrast with a prevalence of hypertension of 2.8% in the total active component in 2013.[7]

Not surprisingly, service members diagnosed with the most severe or complicated forms of glaucoma, angle-closure, glaucoma associated with anomalies or other disorders, and absolute glaucoma, tended to have many more glaucoma-related medical encounters than those service members with less severe or less specific diagnoses. Nearly 35% of those with absolute glaucoma received more than 25 medical visits, as did 17% of service members with glaucoma associated with other disorders, and 7% of those with angle-closure glaucoma.

Most types of glaucoma cause no symptoms until damage to the optic nerve and visual field loss are substantial. For this reason, the National Eye Institute of the National Institutes of Health recommends that individuals with risk factors for glaucoma should receive regular comprehensive dilated eye exams. Those with increased risk include anyone with a family history of glaucoma, those with diabetes or hypertension, and blacks older than 40 years of age. Those not at elevated risk should receive comprehensive eye exams after age 60.[10]

One limitation of this analysis is that an unknown number of the incident diagnoses of borderline glaucoma may reflect a transient elevation of IOP, which, while properly identified during the medical encounter, may never progress to glaucoma, which requires damage to the optic nerve. Therefore, the incidence rates of glaucoma reported here are most likely overestimates of the population truly at risk for advanced disease. It is also possible that many service members diagnosed with borderline glaucoma did not receive a subsequent diagnosis with a more advanced form of the disease during the period covered by this analysis because of the slow nature of the progression of the disease and the fact that many separate from service before the disease becomes problematic.

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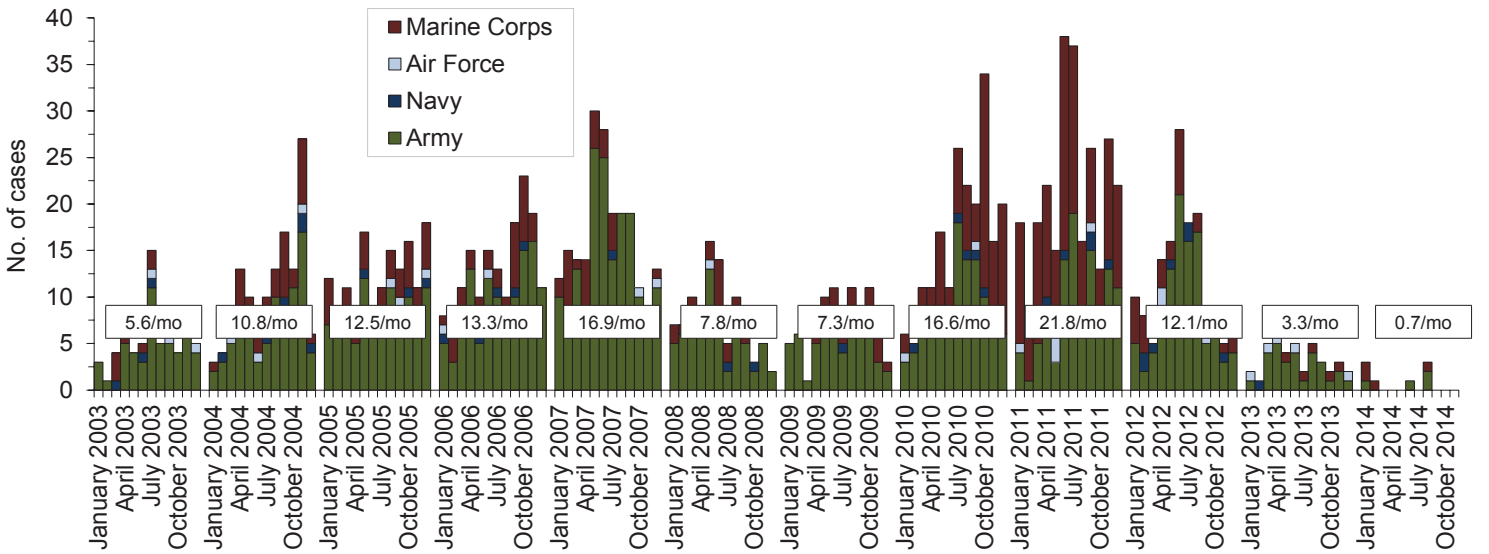
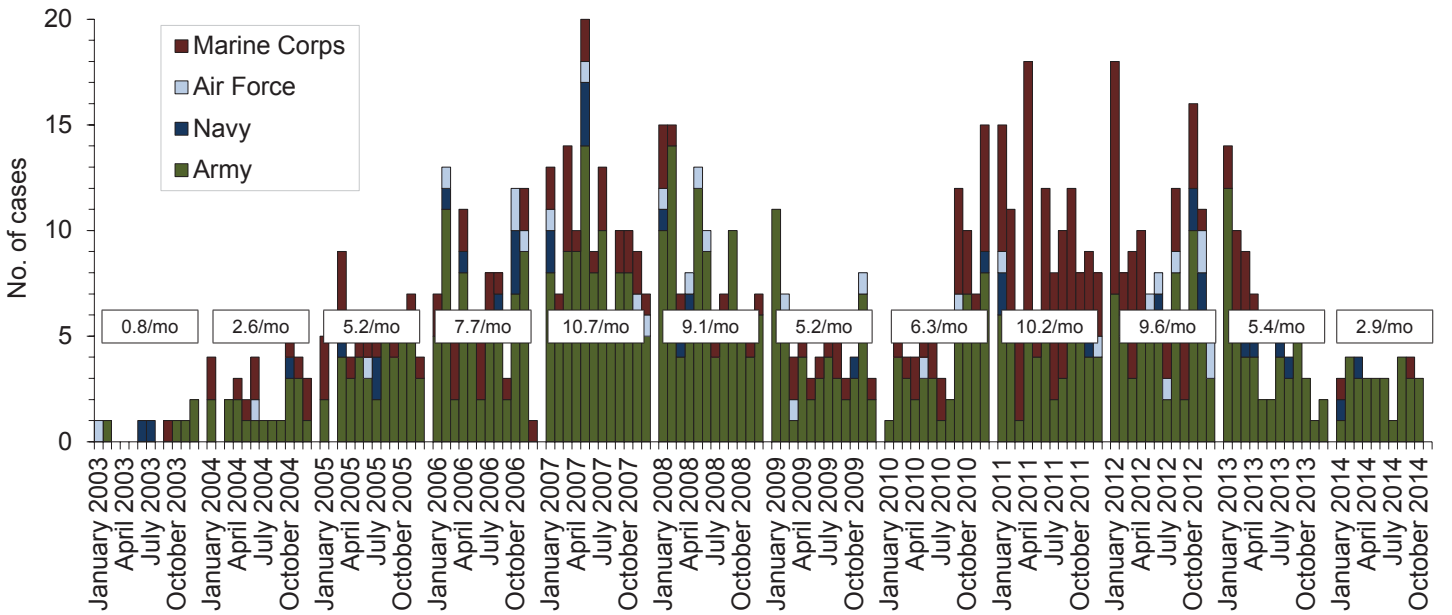
Deployment-related Conditions of Special Surveillance Interest, U.S. Armed Forces, by Month and Service, January 2003–November 2014 (data as of 18 December 2014)

Amputations (ICD-9-CM: 887, 896, 897, V49.6 except V49.61–V49.62, V49.7 except V49.71–V49.72, PR 84.0–PR 84.1, except PR 84.01–PR 84.02 and PR 84.11)[a]



Reference: Army Medical Surveillance Activity. Deployment-related condition of special surveillance interest: amputations. Amputations of lower and upper extremities, U.S. Armed Forces, 1990–2004. *MSMR*. Jan 2005;11(1):2–6.
[a]Indicator diagnosis (one per individual) during a hospitalization while deployed to/within 365 days of returning from deployment.

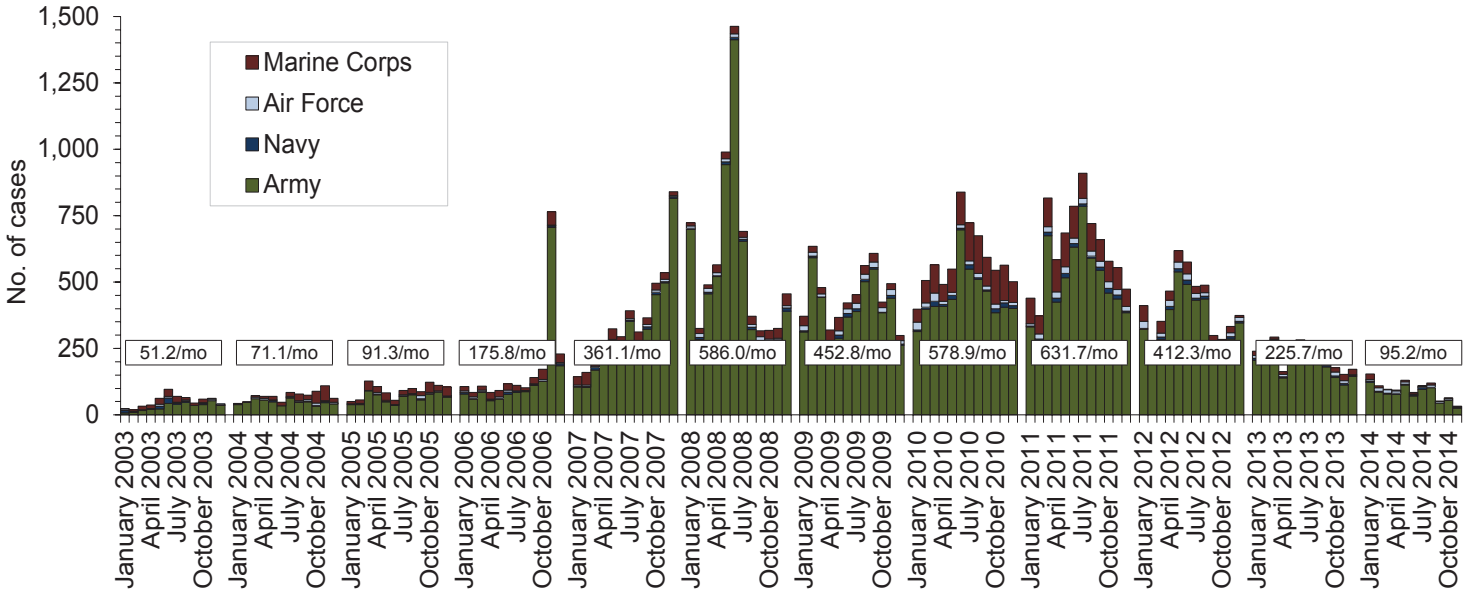
Heterotopic ossification (ICD-9: 728.12, 728.13, 728.19)[b]



Reference: Army Medical Surveillance Activity. Heterotopic ossification, active components, U.S. Armed Forces, 2002–2007. *MSMR*. Aug 2007; 14(5):7–9.
[b]One diagnosis during a hospitalization or two or more ambulatory visits at least 7 days apart (one case per individual) while deployed to/within 365 days of returning from deployment.

Deployment-related Conditions of Special Surveillance Interest, U.S. Armed Forces, by Month and Service, January 2003–November 2014 (data as of 18 December 2014)

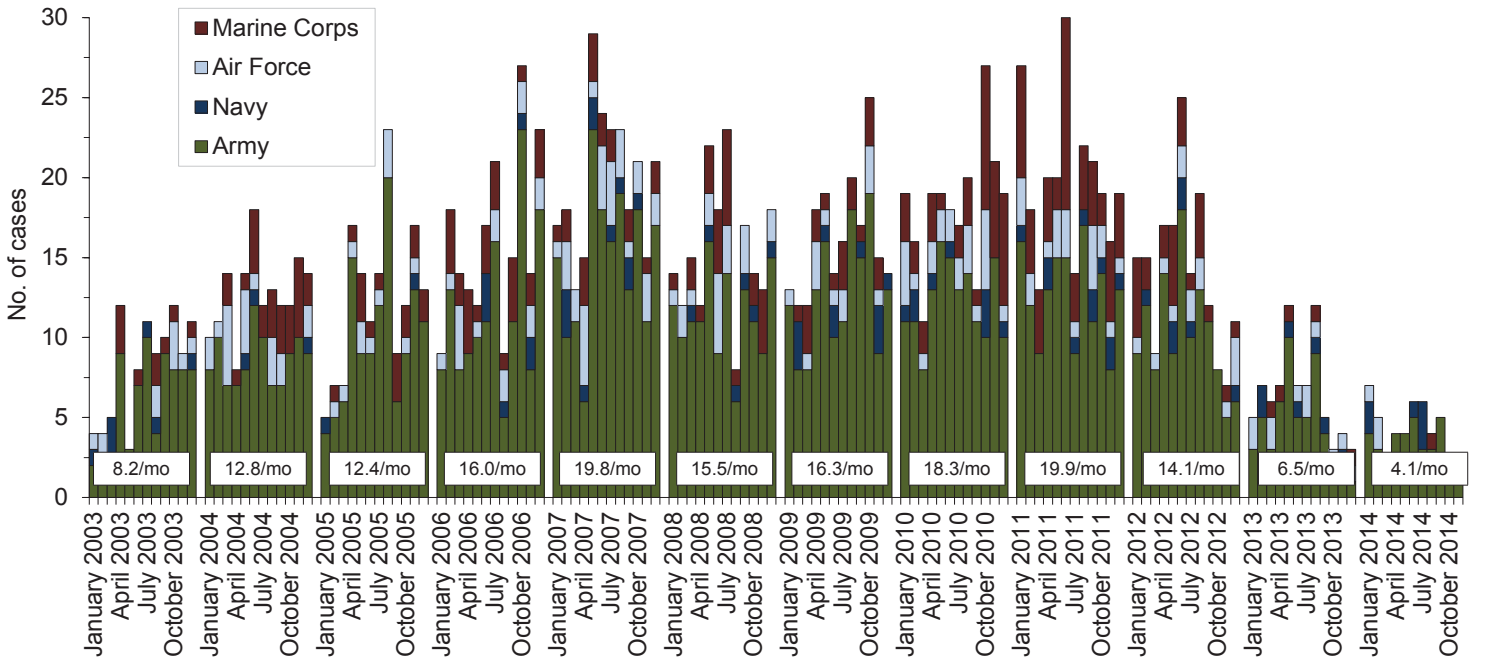
Traumatic brain injury (TBI) (ICD-9: 310.2, 800–801, 803-804, 850–854, 907.0, 950.1–950.3, 959.01, V15.5_1–9, V15.5_A–F, V15.52_0–9, V15.52_A–F, V15.59_1–9, V15.59_A–F)[a]



Reference: Armed Forces Health Surveillance Center. Deriving case counts from medical encounter data: considerations when interpreting health surveillance reports. *MSMR*. 2009; 16(12):2–8.

[a]Indicator diagnosis (one per individual) during a hospitalization or ambulatory visit while deployed to/within 30 days of returning from deployment (includes in-theater medical encounters from the Theater Medical Data Store [TMDS] and excludes 4,508 deployers who had at least one TBI-related medical encounter any time prior to deployment).

Deep vein thrombophlebitis/pulmonary embolus (ICD-9: 415.1, 451.1, 451.81, 451.83, 451.89, 453.2, 453.40–453.42 and 453.8)[b]

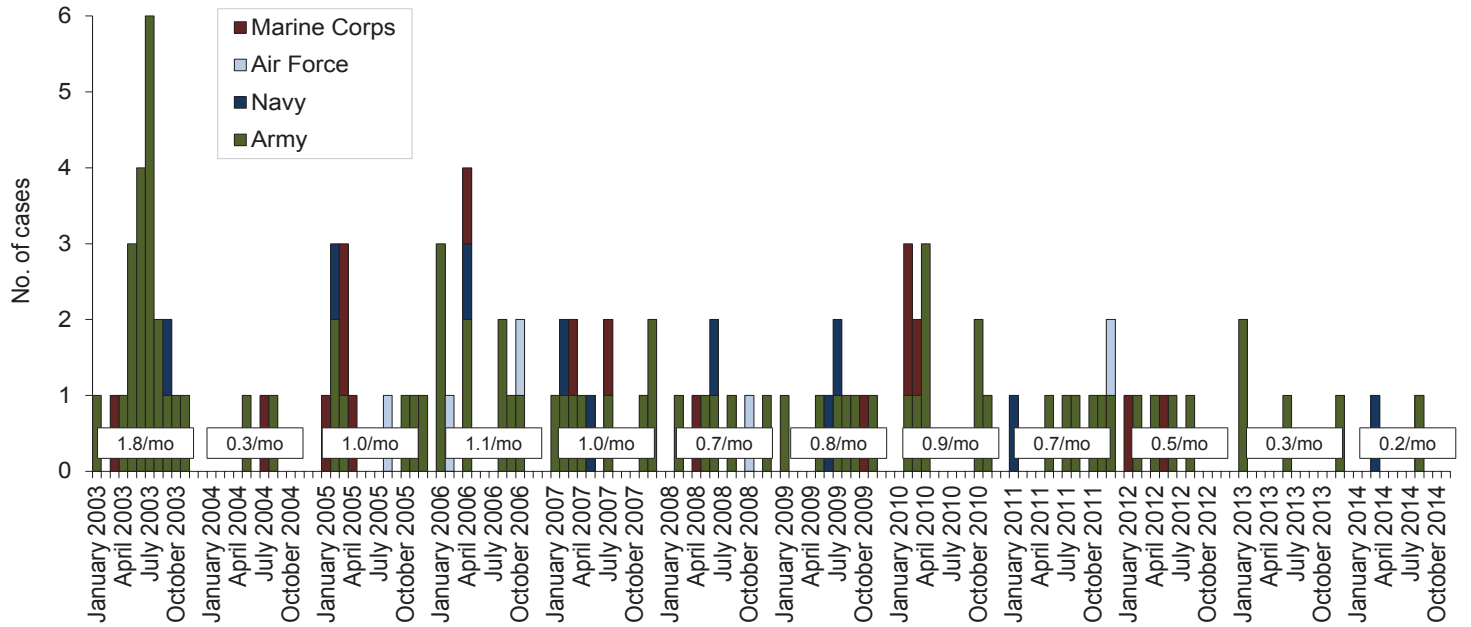


Reference: Isenbarger DW, Atwood JE, Scott PT, et al. Venous thromboembolism among United States soldiers deployed to Southwest Asia. *Thromb Res*. 2006;117(4):379–383.

[b]One diagnosis during a hospitalization or two or more ambulatory visits at least 7 days apart (one case per individual) while deployed to/within 90 days of returning from deployment.

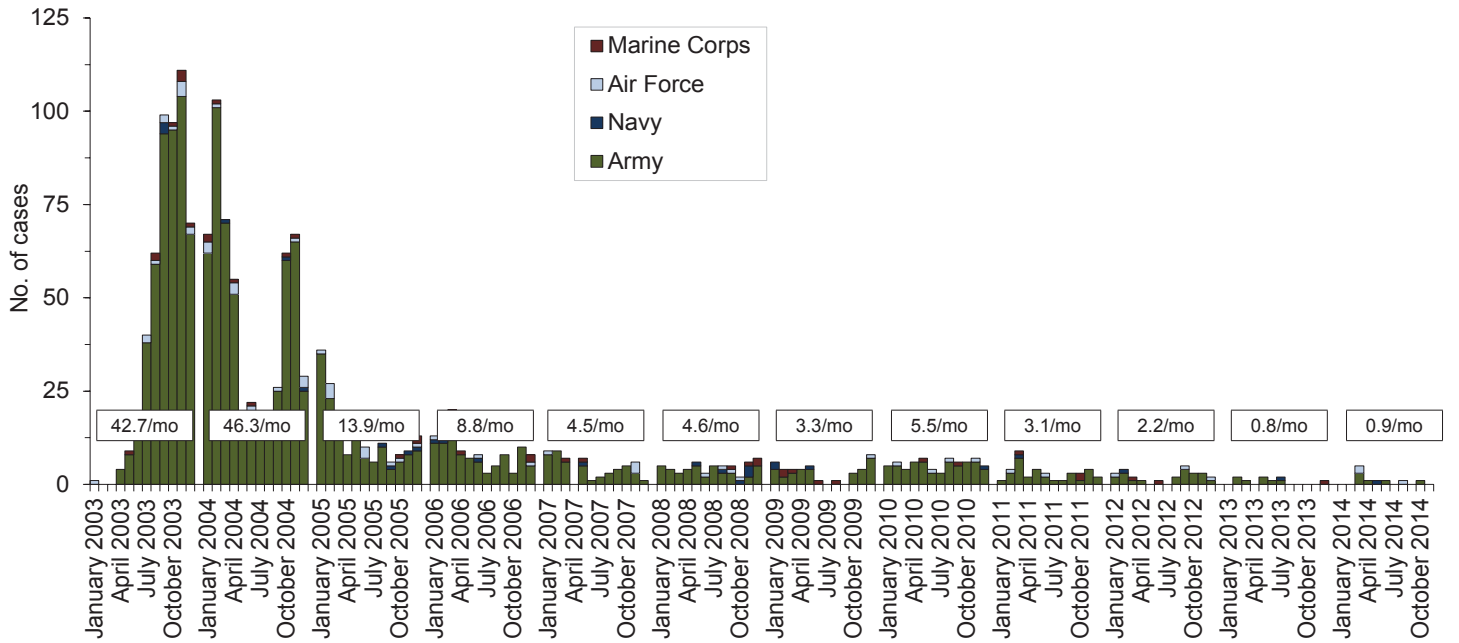
Deployment-related Conditions of Special Surveillance Interest, U.S. Armed Forces, by Month and Service, January 2003–November 2014 (data as of 18 December 2014)

Severe acute pneumonia (ICD-9: 518.81, 518.82, 480–487, 786.09)[a]



Reference: Army Medical Surveillance Activity. Deployment-related condition of special surveillance interest: severe acute pneumonia. Hospitalizations for acute respiratory failure (ARF)/acute respiratory distress syndrome (ARDS) among participants in Operation Enduring Freedom/Operation Iraqi Freedom, active components, U.S. Armed Forces, January 2003–November 2004. *MSMR*. Nov/Dec 2004;10(6):6–7.
[a]Indicator diagnosis (one per individual) during a hospitalization while deployed to/within 30 days of returning from OEF/OIF/OND.

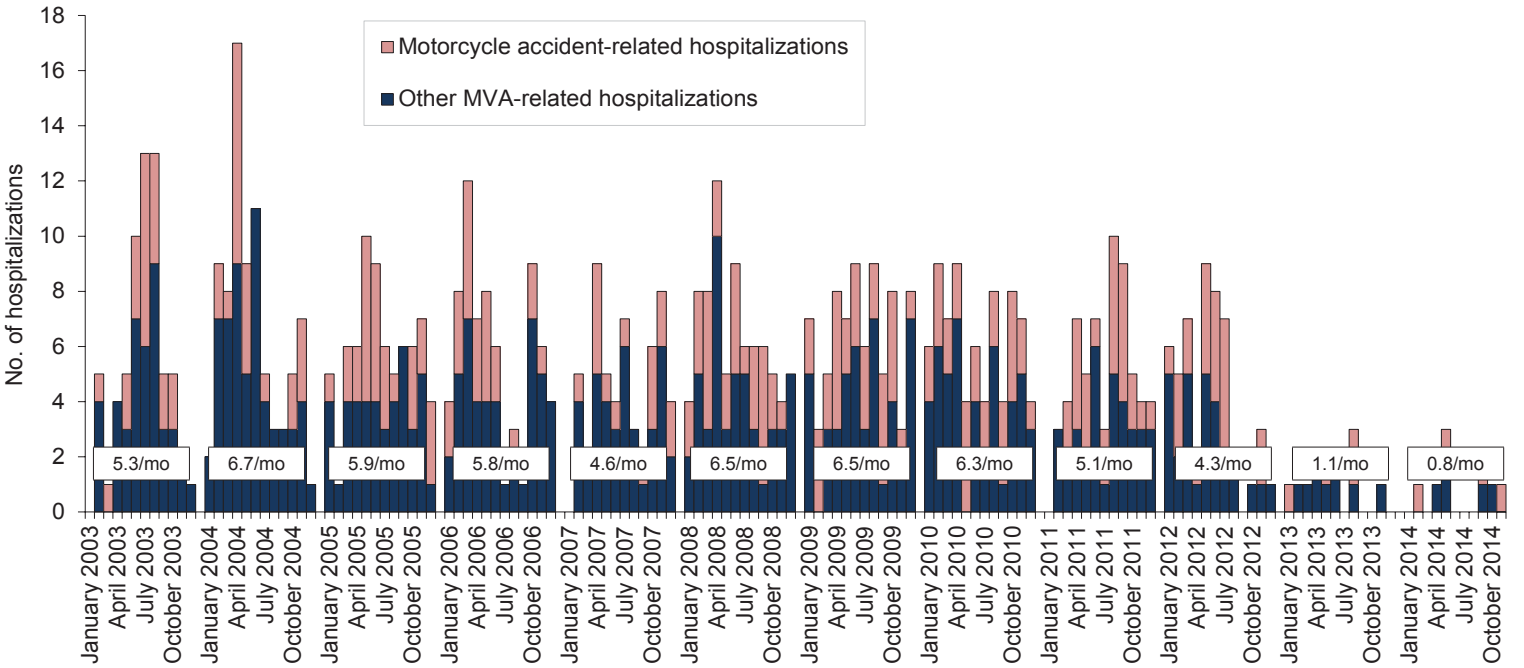
Leishmaniasis (ICD-9: 085.0–085.9)[b]



Reference: Army Medical Surveillance Activity. Deployment-related condition of special surveillance interest: leishmaniasis. Leishmaniasis among U.S. Armed Forces, January 2003–November 2004. *MSMR*. Nov/Dec 2004;10(6):2–4.
[b]Indicator diagnosis (one per individual) during a hospitalization, ambulatory visit, and/or from a notifiable medical event during/after service in OEF/OIF/OND.

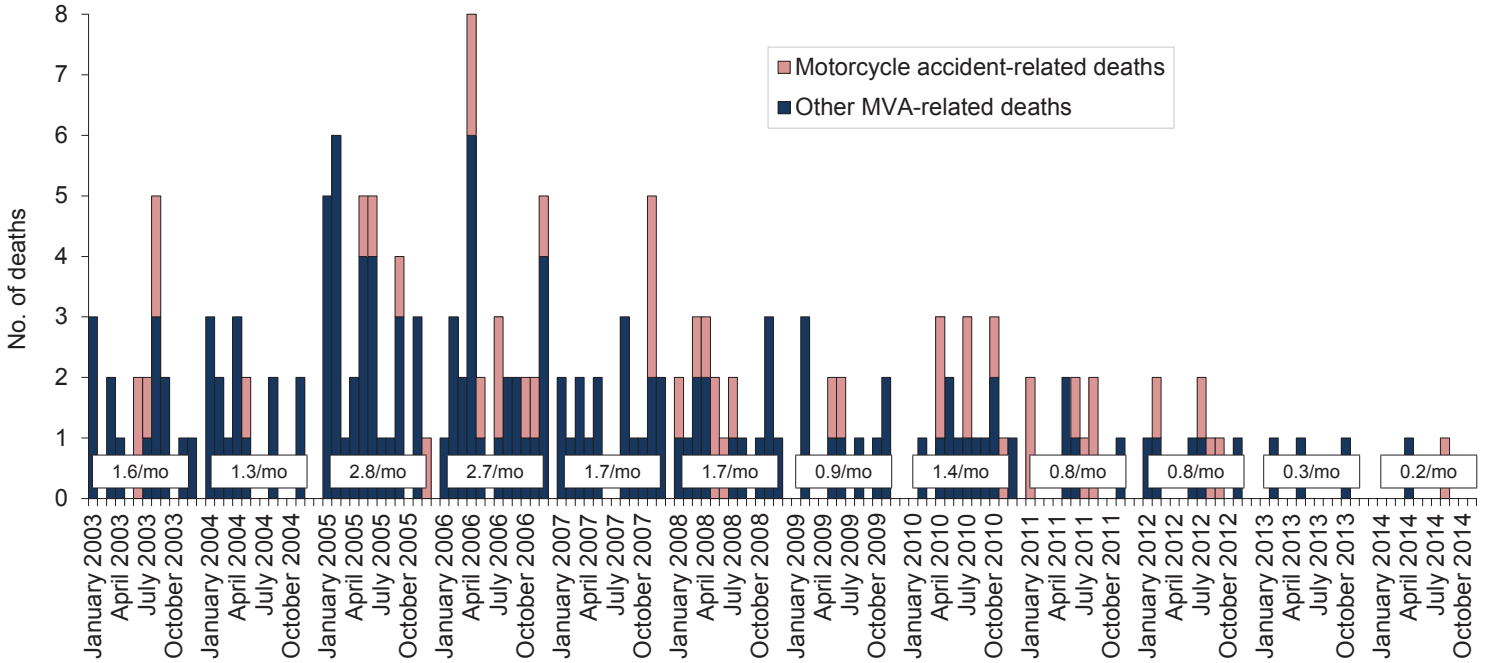
Deployment-related Conditions of Special Surveillance Interest, U.S. Armed Forces, by Month and Service, January 2003–November 2014 (data as of 18 December 2014)

Hospitalizations outside of the operational theater for motor vehicle accidents occurring in non-military vehicles (ICD-9-CM: E810–E825; NATO Standard Agreement 2050 (STANAG): 100–106, 107–109, 120–126, 127–129)



Note: Hospitalization (one per individual) while deployed to/within 90 days of returning from OEF/OIF/OND. Excludes accidents involving military-owned/special use motor vehicles. Excludes individuals medically evacuated from CENTCOM and/or hospitalized in Landstuhl, Germany, within 10 days of another motor vehicle accident-related hospitalization.

Deaths following motor vehicle accidents occurring in non-military vehicles and outside of the operational theater (per the DoD Medical Mortality Registry)



Reference: Armed Forces Health Surveillance Center. Motor vehicle-related deaths, U.S. Armed Forces, 2010. *MSMR*. Mar 2011;17(3):2–6.
Note: Death while deployed to/within 90 days of returning from OEF/OIF/OND. Excludes accidents involving military-owned/special use motor vehicles. Excludes individuals medically evacuated from CENTCOM and/or hospitalized in Landstuhl, Germany, within 10 days prior to death.

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